

Can the Vielight X-Plus be a Therapeutic Intervention for COVID-19 Infection?

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Abstract

This paper proposes the use of Vielight X-Plus as a therapeutic intervention to address COVID-19. The device is based on the science of photobiomodulation (PBM), utilizing red and near infrared (NIR) light to modulate body functions. Fundamentally, PBM involves light of specific wavelengths acting on the respiratory chain of the mitochondria which then triggers higher-level, homeostasis restorative functions. In the process, PBM also improves the immune system to potentially attack viruses and help respiratory diseases. Light from ultraviolet to infrared may destabilize the envelope structures of coronaviruses, increasing the effectiveness of PBM. During PBM, nitric oxide is also released, which inhibits the replication of coronaviruses. PBM also reduces the risks of cytokine storm and sepsis associated with the uncontrolled activity of the immune system as the body fights the disease. The Vielight X-Plus was designed to take advantage of these mechanisms that could make it effective to address COVID-19. It has the added advantage of being portable, suitable for home use, and affordable, with the potential for prophylaxis. It now warrants a randomized controlled study to validate its benefits.

Introduction

COVID-19 is a novel respiratory disease and hence its pathology is largely unknown at this time – recently published on February 28, 2020 are considered to be in early phase¹, although newer data are expected due to intensive global research. Currently there are no vaccines, monoclonal antibodies, or drugs available for the virus, SARS-CoV-2.² However, due to the novelty of the virus, the existence of any viable treatments remains an unanswered question although drug discovery efforts have dominated the search for a cure.³ Medical devices have remained largely unexplored, except for mechanical ventilation and extracorporeal membrane oxygenation.

This paper is prepared in the context of the current COVID-19 pandemic and proposes a randomized controlled study to test the “Vielight X-Plus” as a treatment for COVID-19. It is currently commercially available as a general wellness device and can be mass-manufactured with a lead time of 2 months. The

technology has the potential for acute response with further potential as a prophylaxis. The X-Plus is based on the science of “photobiomodulation” (PBM), which involves the delivery of red and near-infrared light to the cells of the body from light emitting diodes (LEDs). The field of PBM has a substantial volume of research literature dating back to 1967, about 55 years ago. The device has passed independent electrical safety tests for public use.

Fundamental cellular mechanisms

The fundamental mechanisms of PBM are based on absorption of photons by the mitochondria to modulate cellular functions. The X-Plus delivers light of specific wavelength, power and duration to the body to achieve this. The process involves numerous interacting mechanisms that modulate bodily functions.⁴ One result is the regulation of the immune system.⁵ PBM elevates a weakened immune system, and in a healthy cases, could be prophylactic. The central mechanisms of PBM revolve around stimulating the mitochondrial respiratory chain where a transient release of non-cytotoxic levels of reactive oxygen species (ROS) leads to positive modulation of the immune response. PBM has a regulatory role via crosstalk with nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B) for the management of various conditions, including immune-related ones.⁸ In an immunocompromised system, the chain of activity leads to increased production of appropriate levels of white blood cells, while managing inflammation. In short, the appropriate dose of PBM directed to the mitochondria could positively modulate the immune system to address viral infections.



Figure 1: Vielight X-Plus

The coronavirus membrane protein in its envelope has a higher propensity to absorb light from ultraviolet to infrared. The process could destabilize the virus and makes it particularly amenable to further action of PBM.⁵

A molecule released during PBM is nitric oxide (NO). It is commonly identified with vasodilatation,⁴ and improved blood circulation. However, in the context of COVID-19, its value to potentially to attack viruses is much more consequential.³¹

The Key Success Factor is the Effect on the Immune System

Many different viruses exist, and because they have a high propensity to mutate, this makes them perpetual moving targets for drug and vaccine treatments. Even if a treatment for COVID-19 is found today, we can assume that variants will emerge, which we hope will not be as transmissible or have as high a mortality rate. The coronavirus, SARS-CoV-2 differs substantially from related viruses that cause the common cold including four other types of coronaviruses (OC43, HKU1, NL63, and 229E) and the various influenza viruses.

The human body has repeatedly been shown to have the ability to adapt to the ever-morphing microbes and viruses. The ability to combat the moving targets rests heavily on the state of the immune system. It is therefore sensible to test ways to support and enhance the natural capacity to do this. The PBM modality can support the body's naturally ability to restore functional homeostasis, and in the process enhance the immune response against COVID-19 and future variants. Based on its specifications, the X-Plus may be a suitable choice for a PBM device to support the body in its fight with SARS-CoV-2.

In vitro studies irradiating blood serum samples with light have demonstrated significant proliferation of lymphocytes. A study using red light at 660 nm⁶ increased reactive oxygen species (ROS), a free radical. This suggests that the ROS could have been produced by activated free-floating mitochondria²¹, which then act as signals for the lymphocyte proliferation as a response. It may also suggest that there are naïve common lymphoid progenitor cells present in the blood ⁷ that could be activated by PBM for transformation into mature lymphocytes. There is growing evidence that stem cells are highly responsive to PBM resulting in changes to initiate cell proliferation and induce signaling cascades.⁸

In a seemingly confounding manner, yellow/orange (589 nm) light irradiation of blood serum showed greater lymphocyte proliferation than red (which is used in the X-Plus). In this *in vitro* experiment directly irradiating blood samples in tubes, there was a significant increase in CD45 lymphocytes and natural killer (NK) (CD16, CD56) cells. However, there was no significant change in CD3 T lymphocytes, T-suppressor (CD3, CD8) cells, T-helper (CD3, CD4) cells, and CD19 B lymphocytes.⁹ The yellow/orange light produced more pronounced changes than blue or near infrared.

These *in vitro* experiments are not necessarily representative of *in vivo* body responses. In this regard, another study produced evidence-based arguments that the *in vitro* effects of light for exerting an

antiviral effect is not based on wavelength but on the ability to generate oxygen species such as ROS, which is produced in the PBM process.²⁶ We should therefore recognize tissue barriers to light and give more credence to: 1) action spectrum for PBM, and 2) wavelengths required for tissue penetration. The dose provided by the X-Plus through 633 nm (red) and 810 nm (NIR) light respects these requirements.

Photobiomodulation with the Vielight X-Plus as a Potential Treatment for COVID-19

Health Canada and the FDA have cleared a number of PBM devices for various medical indications. These include a variety of aesthetic applications, tissue healing and pain management. Vielight is currently engaged in a regulatory-reviewed pilot and pivotal clinical trials to investigate the Vielight Neuro RX Gamma for Alzheimer's Disease. The cellular mechanisms at cellular levels allow for these benefits to apply across different organ systems, in higher-level restoration of tissue functions.

The literature suggests that PBM can be applied to many more medical conditions.⁴ Those that involve improving the immune system and the management of excessive inflammation are relevant to treating COVID-19.¹⁰

Below, we discuss specific areas that relate to the immune system, and how the design of the Vielight X-Plus that could address the COVID-19 infection.

Targeting the Thymus Gland, Sternal Bone Marrow and Lungs

Figure 2 below shows how the LED of the X-Plus is positioned to treat the thymus, sternal bone marrow and lungs.

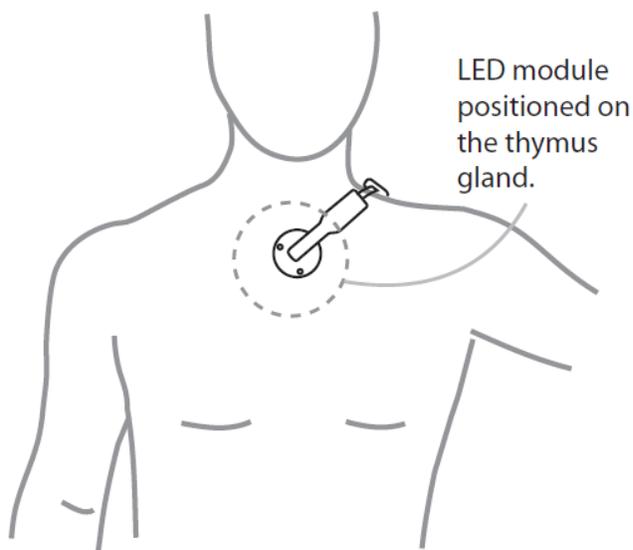


Figure 2: LED module of the X-Plus positioned over the thymus gland

The X-Plus has a NIR LED module placed on the sternum, and from that position, concurrently irradiates the thymus gland, sternal bone marrow and the lungs for PBM effects.

PBM activates stem cell mobilization that leads to tissue repair and production of white blood cells to support the immune system.¹¹ In the case of T-lymphocytes, these are produced in the bone marrow and mature in the thymus gland. Therefore, the application of a controlled dose of PBM to the thymus gland is expected to improve its function and hence improve maturation. Although, the thymus gland loses density as we age, it is rational to believe that it remains active throughout the adult life.^{12 13} Hence the opportunity for thymic stimulation is never lost. PBM can activate the thymus gland and mitigate its reduction throughout its lifespan,¹⁴ as well as activate the surrounding bone marrow to contribute to mesenchymal stem cell genesis.¹⁵ The overall effect helps to boost the immune system to resist a viral infection. An animal study grafting new tissue into aged animals, even showed that reviving the thymus may extend the lifespan – reflecting its importance beyond T-cell support.¹⁶

As evidence pertaining to T-lymphocytes, it was demonstrated in an animal study that PBM irradiation with short treatments at low-level showed elevated IL-2 cytokines, which are products of activated CD4+ T cells. In addition, NO was also produced. However, it should be noted that prolonged use reduced the positive effects, showing that there is a window for optimum results in PBM therapy.¹⁷

Targeting the Respiratory Tract

Viral respiratory infections, such as COVID-19 affects both the upper respiratory tract (nasal cavity, pharynx, larynx) and the lower respiratory tract (trachea, primary bronchi, lungs). The potency of COVID-19 is its ability to migrate to the lung and access the host type II alveolar cells, the most abundant type of alveoli where gas exchanges take place. Its entry is facilitated through the enzyme ACE2 recognized by its “corona” spikes.¹⁸ As the alveolar disease progresses, respiratory failure ensues, and death could follow.¹⁹

The Vielight X-Plus could have a role in intervening the passage of the coronavirus in two ways, by application of:

1. An intranasal LED device in the nasal cavity,
2. A LED module positioned on the thymus gland

Both components of the X-Plus may also contribute an additional beneficial systemic effect that is characteristic of PBM.

Intranasal PBM on Respiratory Infections

Discussion on the effect of intranasal PBM here involves two broad pathways: 1. The systemic effect through irradiating the free-floating mitochondria, and 2. Direct inhibition of the virus through the production of nitric oxide (NO). The intranasal applicator of the X-Plus is used as shown in Figure 3 below. Its LED delivers red light at 633 nm at a safe power density of 6.5 mW/cm².



Figure 3: Intranasal applicator in use

The Systemic Effect of Irradiating the Free-floating Mitochondria

The nasal cavity has been chosen to position an LED for access to the dense local blood capillary networks which are shielded by a very thin light-permeable membrane in the nasal mucosa. This makes it relatively easy for light from the X-Plus LED to reach the blood circulatory system and the requisite tissue. PBM has a body-wide systemic effect mediated by “circulating factors” described in early PBM literature²⁰, but recently identified as free-floating mitochondria.²¹

Therefore, the effect of therapeutic light can be delivered throughout the body by simply irradiating the blood capillaries in the vicinity of the nasal cavity. This effect is circulated and spread throughout the body through the major vessels where blood traverses 50 to 100 cycles an hour.

An early study using a red laser optic fiber to treat vasomotor rhinitis showed a significant increase of T-lymphocytes.²² So the complex and cascading mechanisms that start from the activity of the free-floating mitochondria in blood in the nasal cavity are the likely factors behind boosting T-lymphocyte presence.

Directly Inhibiting Coronavirus through Nitric Oxide Release

Nitric oxide (NO) produced in the nasal passages is possibly part of the defense system against bacterial and viral infections.²³ In viral infections, NO effects are complex and can be protective or deleterious.²⁴ The presence of NO has been found to inhibit the replication of coronavirus.³¹ A PBM applicator, as used by the X-Plus to release of NO this way, would therefore present an opportunity to stop the infection before its migration to the lower respiratory tract where it causes the main damage.

There are suggestions that ultraviolet (UV) C may help to eliminate viruses with direct irradiation²⁵ but prolonged exposure has carcinogenic risks²⁶. Hence recommendation for this wavelength for use in the nasal cavity should be subject to further investigations for safety.

Blue light, which has been found to be anti-microbial is based on disintegrating cellular membrane in bacteria. There is no evidence that it is effective against virus unless an activator such as a singlet oxygen enhancer is introduced²⁷, in which case, toxicity risks emerges when applied internally.

In another application of light, there is research suggesting the use of visible (mainly blue or green) ultrashort pulsed laser (USPL) supported by compelling results for viral inactivation. It is based on resonance action of impulsive stimulated Raman scattering (ISRS) on the viral capsid.²⁸ This is not feasible for practical application for several reasons: 1) The equipment is experimental, large, relatively costly and requires training, 2) The necessity for ultra-short pulsing for viral inactivation has been legitimately challenged,²⁹ 3) It is only effective *in vitro*, 4) SARS-CoV-2 has a layer of envelope in addition to the capsid, which deemed USPL ineffective for this viral strain.

In summary, application of PBM in the nasal cavity with red LED of 633 nm wavelength inhibits coronavirus replication and activates the body's immune response system through whole-body signaling cascades. The wavelength is also in an action spectrum for PBM effects.³⁰ This effect of the X-Plus is supported by scientific literature.⁴

Direct Photobiomodulation of the Lower Respiratory Tract

It is necessary to consider the possibility of direct irradiation of the lower respiratory tract, particularly the lungs where most of the COVID-19 consequential pathology takes place in a symptomatic patient. When positioned on the sternum, the NIR light from the LED module of the X-Plus may reach the lungs See Figure 3.

The earlier discussion on NO having the beneficial effect of inhibiting the replication cycle of coronavirus is also relevant here.³¹

In addition, it has also been found that direct PBM therapy of viral-infected cells has an inhibitory effect when compared to uninfected cells.³² This could have been facilitated by the receptivity of the virus to NIR wavelength.⁵ In another type of viral infection involving herpes simplex virus (HSV), irradiation with PBM also significantly lowered the incidence of local pathology recurrence.³³ Several studies showed

that PBM can lead to increased count of various components of the white blood cell complex, that include macrophages and T-lymphocytes.^{34 35} This points to the benefits of irradiating the lungs directly.

The lungs can become acutely weakened as the COVID-19 progresses. A parallel can be drawn in chronic obstructive pulmonary disease (COPD). In a double-blind study involving COPD patients, PBM therapy of the respiratory muscles was effective in improving acute functional capacity in the patients.³⁶

In summary, positioning the X-Plus module on the sternum allows the benefit of activating the activities of the bone marrow, thymus gland and protecting the lungs. The LED module of the X-Plus for this area emits light of 810 nm. This wavelength was chosen because it has widely been recognized for its penetration depth into mammalian tissues.³⁷

Calming the Cytokine Storm

Accumulating evidence suggests that a subgroup of patients with severe COVID-19 might have a cytokine storm syndrome.³⁸ A “cytokine storm” is an overproduction of immune cells and their secreted cytokines, which is often associated with a surge of activated immune cells into the lungs. The resulting lung inflammation and fluid buildup can lead to respiratory distress and can be contaminated by a secondary bacterial pneumonia – raising the mortality risk of patients.³⁹

In studies, PBM has been shown to promote inflammation through NF- κ B proteins in normal unstimulated cells. However, in the presence of excessive inflammatory markers, PBM has been shown to behave differently. It has been shown to be anti-inflammatory.⁴⁰ The anti-inflammatory characteristic of PBM is expected to calm a potential cytokine storm.

Application in Rehabilitation

Damage to lungs could lead to the risk of sepsis, caused by a weakened immune system continuing on overdrive. Statistics show that half of the survivors of lung sepsis suffer from other infections, kidney failure or cardiovascular problems, i.e. cardiovascular diseases, about three months after the incidence. Furthermore, many sepsis patients suffer severe, long-term functional, cognitive or psychological consequences such as paralysis, depression or anxiety disorders. In 2017, the global burden of sepsis account for 49 million cases and 11 million deaths.⁴¹ In an animal study, the findings suggested that LED application is an inexpensive and non-invasive treatment for lung sepsis that could be effective.⁴²

Application as Prophylaxis

As discussed, PBM has been shown to modulate the body’s own adaptive immune response, both locally and systemically. The literature suggests that PBM may be a viable component in immunotherapy even

for cancer.⁴³ Of relevance to this discussion, the fact that PBM strengthens the innate immune system makes it a credible prophylaxis against diseases, which include viral infections.

Viruses have the propensity to mutate, and we could be potentially facing a “COVID-20 (and beyond)” after this outbreak. Hence the need to continuously support the innate immune system, which in turn also helps with improved adaptive immune response in readiness for the next viral infection. PBM’s support of the body’s innate immunity, inherently provides a simple solution. The X-Plus offers a safe instrument to deliver this.

The usefulness of the intranasal PBM treatment is underlined by new evidence that the loss of smell, or anosmia, and taste are characteristic of about 20 to 59 percent of cases of early COVID-19 infection - making this amongst the strongest predictors of the disease.^{44 45 46} As discussed, the X-Plus intranasal PBM applicator through NO release, may be able to slow down or stop a viral invasion by inhibiting its replication at the nasal cavity, before progressing further into the respiratory tracts.³¹

In summary, the role of intranasal and trans-sternal PBM in prophylaxis for the disease is its potential to improve the body’s innate and adaptive immunity, and to halt viral replication.

Conclusion

In conclusion, several factors support the proposal that the Vielight X-Plus is a viable consideration to address COVID-19.

PBM is supported by a growing amount of research and the evidence that is deep and credible, going back about 55 years.

In relation to the X-Plus:

- It is readily available, with no development time required
- It is commercially available as a general wellness device with a 2-year track record
- Positive anecdotal reports of improved well-being have been received with no safety issues
- The development of the device is based on photobiomodulation (PBM), specifically related to improving the immune constitution
- It is low-cost, portable, does not require training to use and is suitable as a home-use device
- Its design is based on established scientific principles, supported by related empirical evidence.

However, there are certain qualifications:

- Its efficacy needs to be validated in a clinical study
- Although PBM is rapidly gaining scientific recognition, many authorities remains skeptical, which can be corrected with education
- Volume production would require a lead time of two months.

The device warrants a clinical trial. Notwithstanding, the X-Plus present a promising non-invasive solution to attack the COVID-19 virus. This is supported by a body of related literature, history in the market and safety.

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