

Effects of Biophotonic Treatment on Hemoglobin A1c and Blood Oxygen Saturation

Brief Communication

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Abstract

Multiple biochemical events connected to UV irradiation from sunlight or other sources may induce either beneficial or damaging effects on tissue viability. The biophysiological impact is dependent on the wavelengths encountered, the intensity and duration of the exposure, and the tissues exposed whether in vivo or in vitro as an extracorporeal exposure typical of that which is obtained following UV irradiation of freshly obtained heparinized whole blood. The applications of biophotonic therapy have been in use for nearly a century where its use has been found to be highly beneficial in the treatment of both infectious diseases of viral and microbial origin, in addition to enhancing immune responses, oxygenation of peripheral tissues and facilitating tissue regeneration and wound healing in a broad spectrum of disorders. In a short clinical trial, non-diabetic otherwise healthy subjects (n=8) were administered replicate biophotonic treatments during a single day, consisting of the timely reinfusion of 60 ml of heparinized, UV-exposed blood through a specialized quartz mixing cylinder during which the UV exposure occurred. The UV exposure occurred over a ~15-minute duration. Two hours after exposure, blood SpO₂ remained increased by an average of 5% and hemoglobin A1c remained decreased by a similar proportion following completion of the biophotonic treatments. These results suggest that the biophotonic treatment contributed to an acute photodissociation of oxygen from oxyhemoglobin which may improve oxygen delivery to peripheral tissues, in concert with modest improvements in hemoglobin A1c as an indicator of glycemic control. Moreover, in related studies, the effects of biophotonic therapy on SpO₂ have been reported to persist for at least one month following the treatment. Thus, the beneficial effects of UV-biophotonic treatment on HbA1c and SpO₂ persist for at least 2 hours to 4 weeks following treatment, resulting in a broad spectrum of beneficial effects on health and vitality.

Keywords

Diabetes, Hemoglobin A1c, Oxygen Saturation, Biophotonics.

Introduction

Historically, it is noteworthy to recall that sunlight exposure provides UV light irradiation and has empirically been considered nature's all-natural cure-all for infectious illnesses and other disorders for many generations of humankind [1]. The earliest reference of the beneficial

effects of sunlight exposure date to on or before 1500 B.C [1]. Exposure to sunlight and its intrinsic energy in the form of photons has long been considered a prerequisite for maintaining good health, and as such, humans have always instinctively sought daylight for many different

kinds of illnesses including infectious illnesses and to promote wound healing [1-4]. The photonic role of the UV radiation from sunlight in activation of pro-vitamin D to a physiologically active form is also now well documented, as is its subsequent contributions to immune functions and wound healing [5]. Although the molecular mechanisms of these photon-mediated, light-derived effects have generally often remained unknown, unconfirmed, or speculative at best with respect to infectious illnesses, emerging findings now point to a nuclear disruptive element that impedes further local replication of the infectious agents, combined with enhancement of immune responses in the UV or sunlight-exposed host [6]. The sun's rays may also induce modest vasodilation, and thus potential improvements in peripheral circulation, substrate delivery and sustainable oxidative metabolism.

According to the first law of photobiology, light absorption requires the presence of a specific biologic photo acceptor molecule or complex that after photonic excitation could induce the activation of downstream signaling pathways to bring about its desired healthful or other responses [7]. The magnitude of the photobiologic effects depend on the intensity, duration, and cumulative dosage of the UV exposure in a typical dose-related manner. Both ionizing and non-ionizing radiation are known to cause mutations in DNA of cells, albeit through different molecular mechanisms [8]. Strong ionizing radiation such as high-energy UV-C, X-rays, and gamma rays can cause single- and double-strand breaks in the nucleotide and nucleoside backbones through the formation of hydroxyl radicals and other biochemical events upon irradiation exposure [8]. In contrast, exposure to non-ionizing radiation can induce the formation of dimers between two adjacent pyrimidine bases of RNA, and in both cases of ionizing or nonionizing exposure the usual consequence is the prevention of further replication of the infectious agent as a result of the genomic damage [8]. The consensus is that if the denaturation of the viral genetic material occurs, rather than denaturing or damage to the protein and lipid envelopes, it is likely to be the primary and the more efficacious target for an irradiation-induced viral inactivation [8,9]. In contrast, hemoglobin with its porphyrin structure, is an efficient biologic light absorbing photochemical capable of absorbing photons in the 480 nm range of the spectrum [10]. Accordingly, hemoglobin is a likely recipient of biophotonic actions that may result in a relaxation of selected salt bridges following photodissociation of oxygenated hemoglobin, thereby enabling the molecule to transition from its taut (T) to its relaxed (R) state and facilitate the release of oxygen to support intermediary metabolism including wound healing in peripheral tissues [10].

Proposed Mechanisms of UV-biostimulation

The biostimulation process via low level photonic emission generally promotes cell survival and proliferation in both *in vitro* and *in vivo* settings. Emerging evidence supports a low-level laser stimulation action mediates increases in the generation of "good" reactive oxygen species that are able to activate redox sensitive signal transduction pathways such as factors Nrf-2, NF-kB, and ERK [11,12]. Collectively these factors can act as key redox formation checkpoints in cell survival and replication mechanisms that contribute to the proliferation and survival of affected tissues. Because hemoglobin with its porphyrin structure, is an efficient light absorbing photochemical capable of absorbing photons in the 480 nm range of the spectrum, it plays an important role in light-mediated oxygenation reactions. Thus, it is a likely recipient of the biophotonic actions that may reflect an increase in 2,3 BPG, and in photodissociation of oxygenated hemoglobin from its taut (T) to its relaxed (R) state [10-13]. The transition results in a rightward shift in the hemoglobin oxygen saturation curve and contributes to a more efficient release of oxygen to peripheral tissues. Thus, as a result, the bio-stimulation process also improves peripheral oxygen delivery to tissues including tissue myoglobin, via a laser-induced photodissociation of oxygen from oxyhemoglobin in cutaneous blood vessels.

Biophotonic UV treatment improves peripheral blood oxygen saturation kinetics and cell survival

The increased oxygen delivery is presumed to contribute to an increase in blood pO₂ (SpO₂) concentrations and further contributing to its role in the biomedical processes of oxidative substrate metabolism, tissue regeneration and healing [14]. In the process, an improvement in the oxyhemoglobin: deoxyhemoglobin ratio in concert with a gradual decrease in hemoglobin A1c may occur. The increase in SpO₂ may also result in improved capacity for glucose utilization and oxidative metabolism in peripheral tissues and in subsequent improvements in HbA1c via the combined potential effects of reversal or blockade of the non-enzymatic Amadori reaction that is responsible for the glycation reactions, in combination with lower average plasma glucose concentrations [15]. The biophotonics treatment has been reported to result in an improvement in the balance of hemoglobin:hemoglobin-A1c, an important non-enzymatic diagnostic marker utilized in chronic diabetes monitoring, where it can be correlated with mean plasma glucose concentrations over the projected lifespan of the erythrocytes [15].

A summary of the effects of UV and the biophotonic and biophotomodulatory actions on cells, tissues and infectious agents is depicted in Figure 1 below. The potentially damaging effects of extreme exposure as may be caused by excess solar exposure are summarized on

the left side of the diagram, and the proposed effects of extracorporeal biophotonic exposure depicted on the right side of the figure. The blood is typically heparinized during removal to prevent coagulation during the process, quickly diluted in sterile, normal saline and re-infused immediately after brief UV exposure as it travels through a specialized presterilized disposable quartz mixing chamber as outlined previously [16-18]. The process of reinfusion is typically completed within approximately 30 minutes or less of its initial removal from the subject, limited only by the controlled rate of reinfusion. Venous blood samples may be obtained for analysis before and periodically following completion of the process. Blood SpO2 is typically determined with a pulse oximeter during the procedure.

impinged upon by the UV radiation. The content of aromatic residues increases the magnitude of electronic excitement following the absorption of biophotonic energy. Tryptophan (trp) and tyrosine (tyr), with an absorption spectra of 260-290 nm range (peak absorption is 340) are commonly found in most proteins and are a primary target of UV energy. The absorbance spectra are well within the range of the biologically effective spectral range. The duration of the trp fluorescence following UV radiation is of brief duration, however, and while contributory, is thus not likely to be the only component mediating the photodynamic effect and the oxygenic dissociation from hemoglobin [10]. The effects of biophotonics treatment in other skeletal muscle and other tissues remains unclear, but also appears to improve parameters of insulin sensitivity

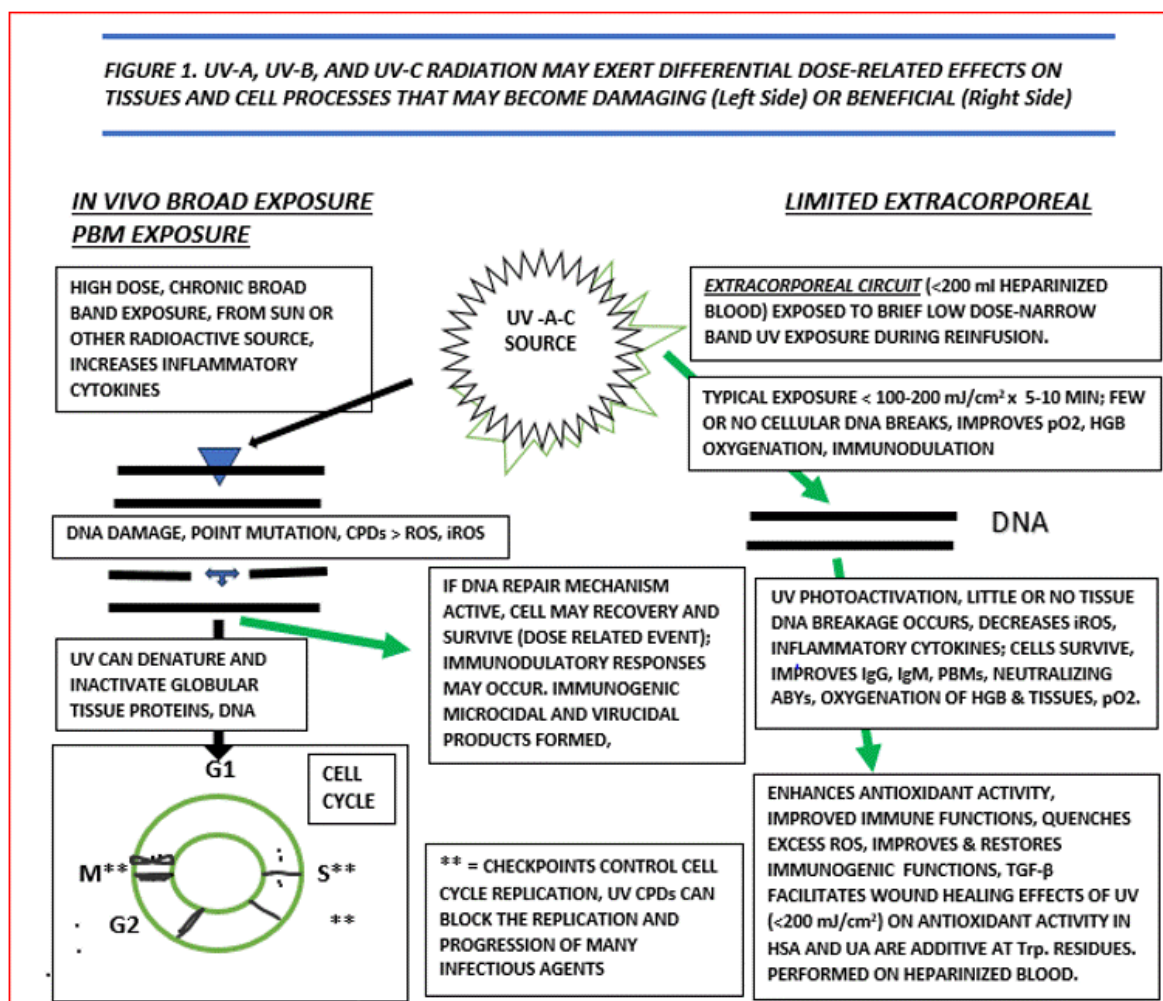


Figure 1: Legend to Figure 1. Summary of the effects of in vivo and extracorporeal UV radiation exposure on tissues and cells. UV = ultraviolet light; UV-A = wavelength 320-400 nm; UV-B= 280-320 nm; UV-C = wavelength 200-280 nm; mJ = millijoules; cm = centimeter; in vivo = in the live organism or subject; CPDs = cyclobutene dimers; ROS = Reactive Oxygen Species; iROS = inflammatory reactive oxygen species; DNA = deoxy nucleic acid; RNA = ribonucleic acid; G1, S, G2 and M = phases of the cell cycle; PBMs = photobiomodulation products; IgG = immunoglobulin G; IgM = immunoglobulin M; ABYs = antibodies; TGF-β =

The effectiveness of the biostimulation effect of UV exposure depends on the aromatic structural residues contained in the protein and nucleic acids of the tissues

and its down range effects of aspects of intermediary tabolism [19].

Fluorescence from RBCs is centered near 480nm, a wavelength common to hemoglobin, and often used in diagnostic procedures to quantify hemoglobin concentrations in blood [10]. Thus, the brief nature and duration of the emission wavelength and fluorescence lifetime allows us to exclude tryptophan as the only primary source of the RBC signal. The signal that resulted in the apparent changes in oxygen dissociation from oxyhemoglobin are likely additive to the trp effects. Nonetheless, the mechanisms associated with the molecular changes in hemoglobin A1c following UV exposure remain unclear. Since the glycation reaction increases the nature of hemoglobin-O₂ affinity and reduces O₂ delivery to peripheral tissues presumably by altering the structure and function of hemoglobin, the biophotonic exposure is likely to decrease hemoglobin glycation. Accordingly, the HbA1c concentrations would be expected to decrease following biophotonic treatment [10-13]. Thus, the purpose of the present paper is to review the effects of biophotonic treatment on hemoglobin A1c and blood SpO₂ concentrations.

Materials and Methods

This review was based on a review of the literature, combined with a brief clinical trial of whole blood UV treatment, with follow-up 120 minutes to one month following completion of the procedure. The subjects of the short study were 8 healthy adults, 4 male and 4 female with no known or pending health issues. All subjects signed consent prior to the study. The study was approved by the Institutional Human Subjects Committee. For the biophotonics treatment. For the bio photonics treatment, 60 ml of venous blood was obtained from a forearm via aseptic procedure in a heparinized syringe (0.25 ml heparin in a 60 ml syringe), then added and gently mixed in a 100 ml normal saline bag for intravenous use. The blood was mixed thoroughly to ensure coagulation did not occur during the interim or during its reinfusion. The blood-saline mixture was then passed through an Azura GHl biophotonic apparatus fitted with 2 UV-A and 2 UV-C light sources with stated luminescence of 3.5 W/cm² (GE 214-UV light allowing quartz tubes, Quartz Tubes, Grand Lodge MI). The quartz chambers were 12 inches long and lined with specialized mixing insertions which enabled the blood to mix and redistribute a total of 15 times during its 12-inch transit through the cuvette. The infusion rate was set at 1.5 drops / minute. The design of the cuvette was such to ensure that all the blood passing thru would receive the same Quanta of UV exposure, regardless if it was near the periphery or central canal region of the cuvette. Venous blood was obtained for HbA1c analysis before and exactly two hours after completion of the procedure. Data were analyzed via Students t test for paired comparisons since each subject acted as their own control [20].

Results

The effects of biophotonic treatment following reinfusion of a 60 ml volume of blood exposed to low level UV irradiation are depicted in Figure 2 and indicate that absolute percentages of HbA1c were modestly decreased 2 hours after the UV treatment was completed. The percentage decrease averaged 5.2 % and was significant at $p < 0.05$ as depicted in Column 3 of Figure 2. The decreases in HbA1c percentage following treatment, although small in absolute magnitude, were also highly significant by paired analysis ($p < 0.05$). The effects of the treatment of SpO₂ are depicted in Figure 3 and indicate that the increase, although also modest in absolute terms was highly significant after 120 minutes. In earlier studies reported by Miley, SpO₂ was elevated after 10 minutes and remained increased for one month following the biophotonics treatment and remained increased after 30 to 120 minutes post treatment [9]. The increase was significant at $p < 0.05$ in both observations. Thus, these changes are consistent with the HbA1c levels depicted above and are suggestive of a physiologic link between the two observations.

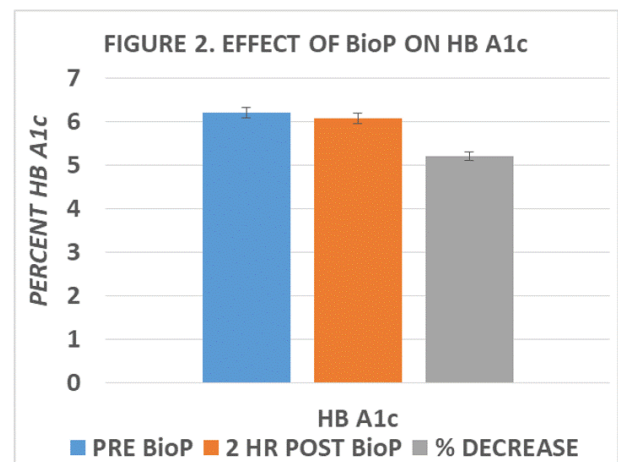


Figure 2: Effect of biophotonic treatment on hemoglobin A1c before and 2 hours post treatment. The percent decrease in hbA1c is depicted in the right column. Data are mean \pm 1 SEM, n= 8 subjects per treatment group. BioP = biophotonics treatment. $P < 0.05$ (Students 't' test for paired variables).

Emerging evidence supports a low-level laser stimulation action mediates increases in the generation of "good" reactive oxygen species that are able to activate redox sensitive signal transduction pathways such as factors Nrf-2, NF-kB, and ERK [12,21,22]. Collectively these factors can act as key redox formation checkpoints in cell survival and replication mechanisms that contribute to the proliferation and survival of affected tissues (Figures 3 & 4).

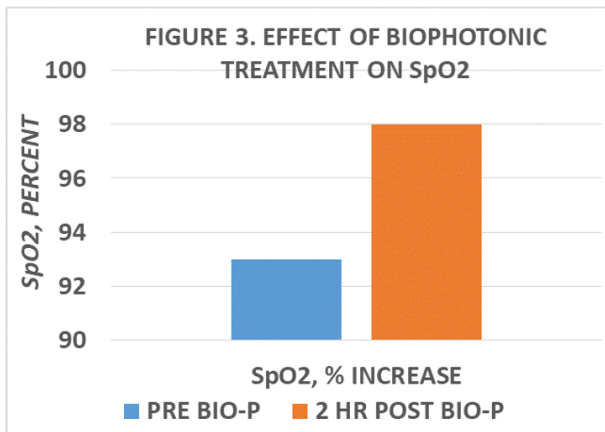


Figure 3: Effect of biophotonic treatment on SpO2 before and 2 hours post treatment. The percentage decrease in SpO2 over 2 hours is depicted in the right column. Data are mean \pm 1 SEM, n= 8 subjects per treatment group. Data are extrapolated from (7). BioP = biophotonics treatment. P = < 0.05 (Students 't' test for paired variables).

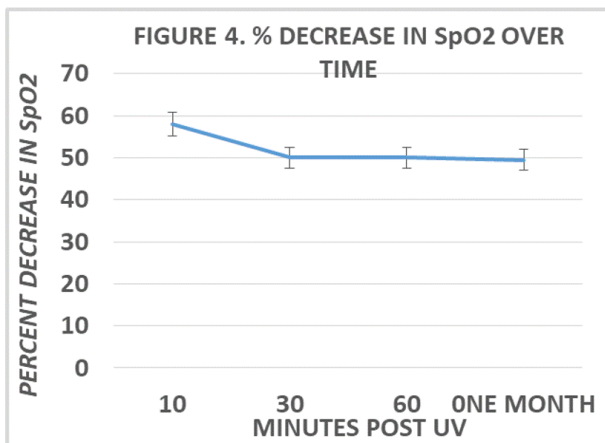


Figure 4: Effect of biophotonic treatment on SpO2 from 10 minutes to one month post treatment. The percentage decrease in SpO2 over 2 hours is depicted in the right column. Data are mean \pm 1 SEM, n= 97 subjects per treatment group. Data are extrapolated from Miley (8).

Discussion and Conclusions

The results of this study indicate that biophotonic treatment results in increases in blood SpO2 in association with a trend toward a decrease in hemoglobin A1c in healthy, non-diabetic subjects. Of interest, the two subjects had HbA1c levels higher than normal range (7.73 vs 7.30, avg decrease also 5.3%), suggestive of a prediabetic state, and those individuals demonstrated the greatest absolute decrease in HbA1c (0.43%). It remains unclear if the biophotonics treatment would be as effective in lowering HbA1c in individuals with longstanding established diabetes as normally the duration to lower HbA1c levels following conventional therapeutic regimens in diabetics may take a month or longer to yield effective results. Further study in a diabetic population with biophotonics as monotherapy or conventional+biopotronics therapy would clearly be of interest.

Hemoglobin is an efficient light absorbing pigment due in part to the porphyrin rings and tryptophan and tyrosine aromatic residues, both of which respond to the UV irradiation range generated by the biophotonic apparatus. While greater magnitude of irradiation may produce damaging effects via both ionizing and non-ionizing induced mutations in cellular components, the damage appears to be irradiation dose related. Cellular damages include double strand breaks in the nucleotide and nucleoside backbones, thymidine dimers, the formation of hydroxyl radicals, ROS, and other biochemical events upon irradiation, which prevent further replication in infectious species. In contrast, the low doses of radiation generated via UV blood irradiation with a low-level laser stimulation action mediates increases in the generation of “good” reactive oxygen species that may be able to activate redox sensitive signal transduction pathways such as factors Nrf-2, NF-kB, and ERK. Collectively these signal transduction factors facilitate key redox formation checkpoints in a cell’s survival and replication mechanisms that contribute to the survival, proliferation, and regeneration of affected tissues. In addition, the low-level irradiation stimulates the immune functions including increased activation of vitamin D3 and improved blood oxygen levels, which improve neutrophil and monocyte detoxification functions. While measures of resting metabolic rates have not been determined during or following biophotonic treatment, the greater oxygen availability could be expected to improve oxidative metabolism of glucose and insulin sensitivity in skeletal muscle and other tissues, with an increase in R.Q. that may approach 1.0. Additional metabolic benefits of improved oxidative metabolism likely include a decrease in the generation of inflammatory cytokines and their pathophysiologic sequela. In addition, in recent studies with an obese mouse strain, Gong et al observed that application of photo modulation treatment was followed by an amelioration of the hyperinsulinemia, insulin resistance, and hyperglycemia in the obese phenotype, where it was associated with an activation of cytochrome C and protein kinase B in skeletal muscle, where a major proportion of the insulin resistance of the animal model typically resides [19]. While direct comparisons are limited between animal and human studies are limited, the basic elements of the biochemical pathways of carbohydrate metabolism and glycemic regulation in humans and rodents are similar [23,24].

In conclusion, the increase in SpO2 is believed to be the direct result of photodissociation of oxygen from oxyhemoglobin. This could enable hemoglobin to transition from the taut ‘T’ to the relaxed ‘R’ form, followed by a shift in the oxygen saturation curve to the right, with corresponding improvements in oxygen availability to peripheral tissues. Miley also reported an increase in peripheral vasodilation, which could further enhance oxygen delivery to peripheral tissues. Biophotonic therapy

has also been reported to increase production of 2,3 DPG, an additional factor in favoring hemoglobin oxygenation kinetics. Regardless of the central mechanism, the effects of biophotonic treatment results in persistent improvements in HbA1c, SpO2 and functional immune capacity, which not only assist in the eradication of a broad variety of infectious agents but contribute to favorable improvements in parameters of intermediary metabolism. Einstein et al. have reported the beneficial effects of biophotonic therapy in effectively resolving hepatitis C, HIV, and MRSA in less than a month of repeated treatments, where it was a cost-effective alternative to traditional chemical-based therapies. In conclusion, when the sundrenched environment or classical pharmacotherapy aren't enough to resolve the symptoms, further studies with bio photonics applicationst in man and animals may come to the rescue.

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References

- Sadraeian M, Zhang L, Aavani F, Biazar E, Jin D. Viral inactivation by light. *eLight*. 2022; 2(1): 18.
- Hockberger PE. A history of ultraviolet photobiology for humans, animals, and microorganisms. *Photochem Photobiol*. 2002; 76(5): 561-579.
- Frysh P. (2022). Sunlight and Your Health. United States: WebMD. Available at: <https://www.webmd.com/paul-frysh>.
- Krasnovsky A Jr, Drozdova NN, Roumbal Ya V, Ivanov AV, Ambartzumian RV. Biophotonics of molecular oxygen: activation efficiencies upon direct and photosensitized excitation. *Chin Opt Lett*. 2005; 3(S1): S1-S4.
- Webb AR, DeCosta BR, Holick MF. Sunlight regulates the cutaneous production of vitamin D3 by causing its photodegradation. *Journal of Clinical Endocrinology and Metabolism*. 1989; 68(5): 882-887.
- Patwardhan RS, Checker R, Sharma D, Sandur SK, Sainis KB. Involvement of ERK-Nrf-2 signaling in ionizing radiation induced cell death in normal and tumor cells. *PLoS One*. 2013; 8(6): e65929.
- Miley G. Ultra-violet blood therapy in acute pyogenic infections. In: Proceedings of local branches of the American Societies for bacteriologists, Eastern Pennsylvania Section, 1943. *J Bacteriol*. 1943; 45(3): 303.
- Liebert A, Capon W, Pang V, Vila D, Bicknell B, McLachlan C, Kiat H. Photophysical Mechanisms of Photobiomodulation Therapy as Precision Medicine. *Biomedicine*. 2023; 11(2): 237.
- Rowen RJ. Ultraviolet blood irradiation therapy; the cure that time forgot. *Int J Biosocial Med Research*. 1996; 14(2): 115-132.
- Tuieng RJ, Cartmell SH, Kirwan CC, Sherratt MJ. The Effects of Ionising and Non-Ionising Electromagnetic Radiation on Extracellular Matrix Proteins. *Cells*. 2021; 10(11): 3041.
- Pan L, Wang X, Yang S, Wu X, Lee I, Zhang X, et al. Ultraviolet irradiation-dependent fluorescence enhancement of hemoglobin catalyzed by reactive oxygen species. *PLoS One*. 2012; 7(8): e44142.
- Reeder BJ, Svistunenko DA, Cooper CE, Wilson MT. The radical and redox chemistry of myoglobin and hemoglobin: from in vitro studies to human pathology. *Antioxid Redox Signal*. 2004; 6(6): 954-966.
- Patwardhan RS, Checker R, Sharma D, Sandur SK, Sainis KB. Involvement of ERK-Nrf-2 signaling in ionizing radiation induced cell death in normal and tumor cells. *PLoS One*. 2013; 8(6): e65929.
- Bhagavan NV, Chung-Eun Ha. Function, Metabolism, and Regulation of Organic Phosphates in Erythrocytes. In *Essentials of Medical Biochemistry (Second Edition)*, 2015 Elsevier Pubs. Available at: <https://www.sciencedirect.com/book/9780124166875/essentials-of-medical-biochemistry>.
- Samaja M, Melotti D, Carenini A, Pozza G. Glycosylated haemoglobins and the oxygen affinity of whole blood. *Diabetologia*. 1982; 23(5): 399-402.
- Tulp OL, Einstein GP. Efficacy of Biophotonics as a Therapeutic Adjunct in Resolving Microbial and Viral Infectious Illnesses. Preprints 2023. 2023091794.
- Koenig RJ, Cerami A. Hemoglobin A1c and diabetes mellitus. *Annu Rev Med*. 1980; 31: 29-34.
- Einstein GP, Tulp OL. Integrated Sigma Dynamics Quantum Energy Therapy Presented by Mathematical Function and Matrices in Immunologic Stimulation. *Proceedings The FASEB Journal*. 2017; 31(S1): A9324LB.
- Gong L, Zou Z, Liu L, Guo S, Xing D. Photobiomodulation therapy ameliorates hyperglycemia and insulin resistance by activating cytochrome c oxidase-mediated protein kinase B in muscle. *Aging (Albany NY)*. 2021; 13(7): 10015-10033.
- Bently RE. PhD Thesis, The mechanism of increased oxygenation via bio-photonic therapy. University of Science Arts and Technology, Montserrat. 2015. USAT Publishing (Montserrat). 110 pp.
- Einstein GP, Echavarría L, Tulp OL. Application of Einstein Matrix Medical Treatment for HIV/HCV therapy. *The FASEB Journal*. 2021; 27(S1): 668.4.
- White S. *Lange's Basic & Clinical Biostatistics: Fifth Edition 5th Edition*. 2019. United States: McGraw Hill Publishers. ISBN-13-978-1260455366.
- Zipper LM, McCulhary RT. Erk Activation Is Required for Nrf2 Nuclear Localization during Pyrrolidine Dithiocarbamate Induction of Glutamate Cysteine Ligase Modulatory Gene Expression in Hep G2 Cells. *Toxicological Sciences*. 2003; 73(1):124-134.
- Pan L, Wang X, Yang S, Wu X, Lee I, Zhang X, et al. Ultraviolet irradiation dependent fluorescence enhancement of hemoglobin catalyzed by reactive oxygen species. *PLoS ONE*. 2012; 7(8): e44142.