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Invited Review

Biological effects and medical applications of infrared radiation

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ABSTRACT

Infrared (IR) radiation is electromagnetic radiation with wavelengths between 760 nm and 100,000 nm. Low-level light therapy (LLLT) or photobiomodulation (PBM) therapy generally employs light at red and near-infrared wavelengths (600–100 nm) to modulate biological activity. Many factors, conditions, and parameters influence the therapeutic effects of IR, including fluence, irradiance, treatment timing and repetition, pulsing, and wavelength. Increasing evidence suggests that IR can carry out photostimulation and photobiomodulation effects particularly benefiting neural stimulation, wound healing, and cancer treatment. Nerve cells respond particularly well to IR, which has been proposed for a range of neurostimulation and neuromodulation applications, and recent progress in neural stimulation and regeneration are discussed in this review.

The applications of IR therapy have moved on rapidly in recent years. For example, IR therapy has been developed that does not actually require an external power source, such as IR-emitting materials, and garments that can be powered by body heat alone. Another area of interest is the possible involvement of solar IR radiation in photoaging or photorejuvenation as opposites sides of the coin, and whether sunscreens should protect against solar IR? A better understanding of new developments and biological implications of IR could help us to improve therapeutic effectiveness or develop new methods of PBM using IR wavelengths.

1. Introduction

Infrared (IR) is a type of electromagnetic radiation, including wavelengths between 780 nm and 1000 μm. IR is divided into different bands: Near-Infrared (NIR, 0.78–3.0 μm), Mid-Infrared (MIR, 3.0–50.0 μm) and Far-Infrared (FIR, 50.0–1000.0 μm) as defined in standard ISO 20473:2007 Optics and photonics – Spectral bands [1]. Several studies have reported that IR can improve the healing of skin wounds, photoprevention, relieve pain, stiffness, fatigue of rheumatoid arthritis, ankylosing spondylitis, potentiate photodynamic therapy, treat ophthalmic, neurological, and psychiatric disorders, and stimulate the proliferation of mesenchymal and cardiac stem cells [1–9].

Low-level light therapy (LLLT) is defined as “Treatment using irradiation with light of low power intensity so that the effects are a response to the light and not due to heat. A variety of light sources, especially low-power lasers are used.” in the Medical Subject Headings (MeSH) Descriptor Data 2017. Photobiomodulation (PBM) therapy is “A form of light therapy that utilizes non-ionizing forms of light sources, including lasers, LEDs, and broadband light, in the visible and infrared spectrum. It is a nonthermal process involving endogenous chromophores eliciting photophysical (i.e., linear and nonlinear) and photochemical events at various biological scales. This process results in beneficial therapeutic outcomes including but not limited to the alleviation of pain or inflammation, immunomodulation, and promotion of wound healing and tissue regeneration.” as defined in Anders et al. [10]. It is now agreed that “PBM therapy” is a more accurate and specific term for the therapeutic application of low-level light compared with “LLLT”.

All photobiological responses are determined by the absorption of energy by photoacceptor molecules (chromophores) during light irradiation. It is important to clarify the molecular mechanism of light interactions with tissue by identifying the photoacceptor molecules. IR-induced physiological effects are thought to be due to two main types of photoacceptor (i.e., cytochrome *c* oxidase and intracellular water) [11]. Photon absorption converts light into signals that can stimulate biological processes [12]. The action of IR light on water dynamics in membranes, mitochondria and/or cells could modulate signaling pathways, production of reactive oxygen species (ROS), ATP (adenosine triphosphate), Ca^{2+}, NO, and inositol phosphates group [13–16]. Secondary effects are always preceded by primary effects, including

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stress signaling, metabolic processes, cytoskeleton organization, cell proliferation/differentiation, and homeostasis (depending on injury or metabolic redox potentials) [17,18]. Additionally, Shapiro et al. demonstrated that IR light could excite cells through water absorption, with a temperature increase affecting the plasma membrane and altering the electrical capacitance, thereby depolarizing the target cells [19].

Pollack et al. have demonstrated that water in specific locations within cells exists as a more chemically/biologically active molecule [20]. Most intracellular water is dynamic and has an ordered structure to support the life processes in biological systems [21]. Since the water electromagnetic absorption spectrum is mainly in the IR region, photon absorption can result in a rapid increase in intracellular temperature [22], which may promote unwanted physiological changes in temperature, pH, osmosis, and ATP yield [23,24].

For billons of years, the sun has generated IR radiation and living organisms on earth have evolved to deal with IR radiation as an important environmental factor depending on their habitat. Many ancient therapies have applied sunlight for wound healing and pain relief. The spectrum of sunlight in the environment and the corresponding water absorption spectrum are shown in Fig. 1 [25]. It is clear that the solar emission and the strong water absorption bands are nearly matched. Before sunlight penetrates the atmosphere, it is presents a more uniform emission spectrum. While sunlight reaches the ground, some bands have been absorbed by environmental gas or water molecules in the atmosphere. Since the human body is made up of 70% water, it can potentially accumulate a large amount of energy that could modulate biological processes, by strong resonant absorption of IR radiation from sunlight mediated by water molecules.

In recent years, the combination of technical, clinical, and photobiological principles have become important to understand the therapeutic effects of LLLT. For example in recent years, optical fiber delivery systems have become an important technology to facilitate LLLT [26]. Fiber-optics can transmit light at specific wavelength over long distances by utilizing total internal reflection, allowing them to bend along its path and focus the emission spot on a specific area. Although the light delivery procedures needed for LLLT to be used for diseases of the lungs and airway are difficult, optical fibers inside needles can be applied [27].

In addition, non-invasive, long-range, energy delivery has been described using an infrared-pulsed laser device (IPLD) of 904 nm pulsed at 3 MHz, which was claimed to have an original mechanism of action termed "photo-infrared pulsed bio-modulation" (PIPBM). The device was applied in a clinical trial of advanced cancer patients and a case of age-related macular degeneration (geographic atrophy) with associated neurological disease, it demonstrated sufficient evidence for its selective, long-distance, reparative and/or regenerative physiological effects [16,28,29].

Previous clinical studies have shown that LLLT has a wide range of benefits on various patient populations, different medical indications and conditions without any serious risk of adverse effects. Adequate dosimetry is important for LLLT and PBM therapy; a basic principal has emerged called the "biphasic dose response", where larger doses of light have been found to be less effective than smaller doses [30]. This phenomenon is seen in the beneficial neurological effects of transcranial LLLT for traumatic brain injury, where the results vary significantly depending on the number of treatments and the energy density of each individual treatment.

The present review paper will only summarize some of the key studies about the new application and scientific findings related to IR radiation. It will particularly focus on the new applications, including IR emitting materials for clothing, IR sauna therapy, Waon therapy etc. In addition, we present some newly-emerged scientific findings about neural stimulation, photoaging, photorejuvenation, antitumor action, neural and adipose regeneration.

2. New Development and Application of Infrared Therapy in Biological Fields

2.1. Infrared Emitting Materials for Clothing

In recent years nanotechnology development has provided functional sportswear with many properties to enhance sports activities, performance, efficiency and comfort. For example, sportswear should allow the wearer to stay warm in cold environment, and keep cool in hot situations through transferring sweat away from the skin. In general, the mechanism of action of IR radiating materials is to transform heat energy from the body (convection and conduction) into radiation within the IR wavelength range between 3 and 20 μm to induce homeostasis and photobiomodulation via deeper penetration of IR radiation and water molecule absorption in the skin [25]. The use of materials that generate IR radiation is possibly helpful to enhance blood circulation and the metabolism of human body. Previous studies have found that the effects of IR can activate fibroblasts, increase more collagen synthesis and the expression of transforming growth factor-beta1 (TGF-beta1) in rat wounds [31].

Previous studies have found that the incorporation of nanoscale germanium (Ge) and silicon dioxide (SiO_2) particles into composite

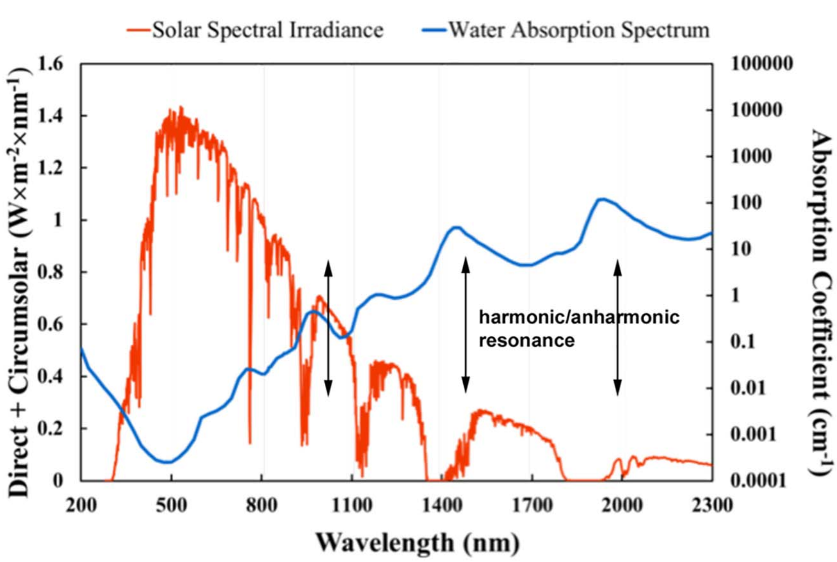

Fig. 1. Superposition of spectra of solar irradiance and water absorption showing that the most significant areas of overlap occur in the region of 800–1300 nm.