

The question that immediately arises is, "How can light, when externally applied, be capable of inducing such a phenomenal effect at the cellular level?" Well, the answer is best explained using the basic principles of photochemistry. Photochemistry is a discipline of chemistry that studies the interaction between atoms, molecules, and light. According to quantum theory, light radiation energy is absorbed as discrete units called photons, and at the molecular level, it is this photon-induced chemistry that ultimately gives rise to the observable effect at the biological level. The first law of photochemistry states that the observable biological effects subsequent to LLLT can only transpire in the presence of a photoacceptor molecule, a molecule capable of absorbing the photonic energy being emitted. A molecule capable of photonic absorption usually contains a light-absorbing center, referred to as a chromophore. Light absorbing centers often house transition metals, elements that are readily identified by their incomplete subshell. Based on physicist Niel-Bohrs model, subshells of an atom identify the possible quantum states in which an individual electron can reside, depending on its energy level. Electrons are capable of undergoing quantum leaps, where an electron transitions between quantum states, shifting from one energy level to another following the absorption or emission of a photon. The shift from a lower energy state to a higher state is referred to as the excitation of an electron, the change from an occupied orbital to a given unoccupied orbital. Regarding transition elements, such as copper (Cu) or iron (Fe), these elements are more susceptible to an electron shift because of their unique electron configuration. The photoacceptor molecules responsible for the photobiological effects subsequent to laser irradiation contain transition metals. The photon absorption is followed by a rapid vibrational relaxation which causes the molecule to reach an equilibrium geometric configuration corresponding to its electronic excited state. This change may modulate the biological behavior of photoabsorbing molecules.

Studies have revealed that cytochrome c oxidase serves as a photoacceptor molecule. Cytochrome c oxidase is a multicomponent membrane protein that contains a binuclear copper center (CuA) along with a heme binuclear center (a₃-CuB), both of which facilitate the transfer of electrons from water soluble cytochrome c oxidase to oxygen. Cytochrome c oxidase is a terminal enzyme of the electron transport chain and plays a vital role in the bioenergetics of a cell. Studies indicate that following laser irradiation at 633nm, the mitochondrial membrane potential and proton gradient increases, causing changes in mitochondria optical properties, increasing the rate of ADP/ATP exchange. It is suggested that laser irradiation increases the rate at which cytochrome c oxidase transfers electrons from cytochrome c to dioxygen. Moreover, it has been proposed that laser irradiation reduces (gain of electrons) the catalytic center of cytochrome c oxidase, making more electrons available for the reduction of dioxygen. The photoactivation of terminal enzymes, like cytochrome c oxidase, plays a vital role in the activation of the diverse biological cascade observed subsequent to laser irradiation.

The peak absorption of cytochrome c oxidase is found in the red to near-infrared spectrum. Therefore, optimal biological stimulation can be achieved utilizing a device that emits light within the red spectrum. Furthermore, to ensure proper depth penetration and deep tissue stimulation, the use of a coherent laser source is absolutely vital. Biologically speaking, the difference between a light emitting diode (LED) and laser diode are negligible at extremely superficial surfaces. However, when attempting to target deep tissue, such as subcutaneous adipocytes, it is essential that a coherent laser source is administered.

The initial physical and/or chemical changes of cytochrome c oxidase have been shown to alter the intracellular redox state. It has been proposed that the redox state of a cell regulates cellular signaling pathways that control gene expression. Modulation of the cellular redox state can activate or inhibit signaling pathways such as redox-sensitive transcription factors and/or phospholipase A2. Two well defined transcription factors, nuclear factor Kappa B (NF- κ B) and activator protein-1 (AP-1), are regulated by the intracellular redox state; moreover, NF- κ B and AP-1 become activated following an intracellular redox shift to a more alkalized state.^{32,33} Subsequent to laser irradiation, a gradual shift towards a more oxidized (alkalized) state has been observed; more importantly, the activation of redox-sensitive transcription factors and subsequent gene expression has been demonstrated.

Based on its ability to modulate cellular metabolism and alter the transcription factors responsible for gene expression, low level laser therapy (LLLT) has been found to alter gene expression³⁶, cellular proliferation, intracellular pH balance, mitochondrial membrane potential, generation of transient reactive oxygen species and calcium ion level, proton gradient, and consumption of oxygen. Moreover, the proliferation of keratinocytes and fibroblasts has been reported in the literature for extremely low doses of laser irradiation.

The modulation of transcription factors has become a common therapeutic strategy to prevent or provoke the expression of specific genes, and the approach could potentially provide a means to treat a wide assortment of medical disorders. Jackson and coworkers (2002) identified more than 20 transcription factors that are regulated by the intracellular redox state. It is proposed that laser therapy, because it has been identified to alter the intracellular redox state, could affect the function of transcription factors associated with the formation and maintenance of adipocyte membranes. To support this claim, further studies are highly warranted. However, there is enough evidence to support that laser irradiation within the red spectrum does play a unique role in the expression of specific genes, and is plausible that the transitory pore observed following LLLT could result from the alteration in gene expression.

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