The Mechanism of Phototherapy for *HOPENT*

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Photo-bio-stimulation excites electron transfer in the respiratory chain enzymes, which fuels proton transfer across the membrane of the mitochondria. The energetic protons produced by this procedure fuel the transformation of ADP to the energetic ATP, which in turn fuels the calcium ATPase, an enzyme, which plays the role of a pump that ejects calcium ions out of the cells. Without calcium ions in the cell, the membrane of the histamine containing organelles in the (mast) cell cannot fuse with he membrane of the cell, which makes exocytosis, the expulsion of histamine out of the cell, impossible. In addition to promoting calcium exocytosis, photo-bio-stimulation also inhibits influx of new calcium by blocking the voltage-gated calcium ion channels. This is due to another effect of photo-bio-stimulation: the production of reactive oxygen species. Again light excites electron transfer in an enzyme to an oxygen molecule, the enzyme is located this time in the cell membrane.

This produces a reactive oxygen which produces hydrogen peroxide. Hydrogen peroxide reacts with arginine to give nitric oxide. Nitric oxide combines with guanylate cyclase to produce cyclic guanosine monophosphate (cGMP}. cGMP combines with a cGMP-dependent protein kinase, which opens a K (potassium) ion channel. The entrance of K ions hyperpolarizes the cell membrane. This hyperpolarization blocks the voltage-gated calcium ion channel. The reduced amount of calcium which stops exocytosis in mast cells also causes relaxation in muscle cells, producing vasodilatation in blood vessels. Besides acting against histamine production, photo-bio-modulation also reduces inflammation.

Inflammation is due to reactive oxygen species (ROS) and we have said that photo-bio-stimulation increases ROS production.
This is however a complex process in phagocyte cells, which are the main causes of inflammation since they produce huge amounts of ROS in a burst, called the respiratory burst. How is this brought about? We have said that ROS is produced by an enzyme in the cell membrane. The enzyme molecules need to be assembled. This assembly is activated by the ROS (hydrogen peroxide, to be precise) themselves, which must penetrate from the membrane into the cell for this purpose. So we have an accelerating process here: the more ROS the more ROS-producing enzyme molecules and the more enzyme molecules the more ROS production.

There is however a competing process: the NADPH molecules which fuel the ROS-producing enzymes are exhausted by the ROS production process itself. Moreover, the hydrogen peroxide produced in the process, besides stimulating enzyme assembly, will also attack (oxidize) the NADPH molecules, getting destroyed itself in the process. So if we stimulate an individual enzyme molecules by the photons emitted by the light emitting diodes (LEDs), we increase the hydrogen peroxide concentration and the probability of NADPH together with hydrogen peroxide destruction. Therefore, the respiratory burst in the presence of irradiation will be far less intense, leading more to self-destruction of the phagocytes than to inflammation.

Finally, by its well-known wound-healing action, photo-bio-stimulation repairs the tissues destroyed by the inflammation, thereby decreasing the sensitivity of these tissues to the allergy inducing agents (allergens).