Synergistic Effects of Light Therapy and Nutrition

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Sunlight is a portion of the electromagnetic radiation given off by the Sun
Yellow line = the spectrum of direct illumination under optimal conditions
• Although cells in vitro are responsive to a variety of wavelengths in the electromagnetic spectrum, beneficial responses in vivo are observed within a narrow wavelength range.

• Lower wavelengths such as violet and ultraviolet penetrate less, whereas those in the red and infrared range have higher penetration.

• Energy at wavelengths shorter than 600nm are generally scattered in biological tissues in vivo and are absorbed by melanin, whereas water significantly absorbs energy at wavelengths higher than 1150nm.

• For clinical purposes = the in vivo therapeutic “optical window” strongly corresponds to red and near-infrared wavelengths.
Low-Level-Laser (Light) Therapy (LLLT) involves exposing cells or tissue to low levels of red and near infrared (NIR) light, and is referred to as “low level” because of its use of light at energy densities that are low compared to other forms of laser therapy that are used for ablation, cutting, and thermally coagulating tissue. LLLT is also known as “cold laser” therapy as the power densities used are lower than those needed to produce heating of tissue. It was originally believed that LLLT or photobiomodulation required the use of coherent laser light, but more recently, light emitting diodes (LEDs) have been proposed as a cheaper alternative.
Light Therapy has now developed into a therapeutic procedure that is science-based, well-substantiated, and utilized in three main ways:

1. to reduce inflammation, edema, and chronic joint disorders;
2. to promote healing of wounds, deeper tissues, and nerves;
3. and to treat neurological disorders and pain.
A chromophore is the part of a molecule responsible for its color.\footnote{1}

The color arises when a molecule absorbs certain wavelengths of visible light and transmits or reflects others.

Visible light that hits the chromophore can thus be absorbed by exciting an electron from its ground state into an excited state.
Mitochondria are stimulated, leading to increased ATP production, modulation of reactive oxygen species, and induction of transcription factors.

Patient Benefits Include:

- Increased healing of chronic wounds
- Improvements in sports injuries and carpal tunnel syndrome
- Pain reduction in arthritis and neuropathies
- Amelioration of damage after heart attacks, stroke, and nerve injury
“Photoneuromodulation of cytochrome oxidase activity is the most important primary mechanism of action of LLLT. Cytochrome oxidase is the primary photoacceptor of light in the red to near-infrared region of the electromagnetic spectrum. It is also a key mitochondrial enzyme for cellular bioenergetics, especially for nerve cells in the retina and the brain. Evidence shows that LLLT can secondarily enhance neural metabolism by regulating mitochondrial function, intraneuronal signaling systems, and redox states.”
Cytochrome c oxidase has been shown to have a new enzymatic activity—the reduction of nitrite to nitric oxide.

Low intensity light enhances nitric oxide synthesis by cytochrome c oxidase without altering its ability to reduce oxygen.

From these findings, we propose that cytochrome c oxidase functions in photobiomodulation by producing nitric oxide, a signaling molecule which can then function in both intra- and extracellular signaling pathways.
“We show both in purified systems and in myocardium that R/NIR light can decay nitrosyl hemes and release NO, and that this released NO may enhance the cardioprotective effects of nitrite. **Thus, the photodissociation to NO and its synergistic effect with sodium nitrite may represent a noninvasive and site-specific means for increasing NO bioavailability.**”
(1) NO via the beneficial cNOS pathway is decreased in joint structures exposed to chronic load-induced stresses and biochemical change-induced stresses,

(2) Monochromatic infrared light energy at an 890 nm wavelength, applied at the skin surface, is absorbed into blood vessels and stimulates production of NO in joints by the beneficial cNOS pathway,

(3) NO from the cNOS pathway may help decrease the detrimental effects of NO induced by iNOS and produced in OA pathology, and

(4) NO-based intervention may produce substantial pain relief without undesirable side effects by increasing circulation, decreasing nerve irritation, and decreasing inflammation in joints.
Nitric Oxide (NO) is absorbed by hemoglobin and endothelial cells. 890nm IR causes the photo-dissociation of NO from hemoglobin in the red blood cells (and possibly from the endothelial cells as well) allowing NO to be free (locally) to do its work.
NO Release From Tissue or Blood:

- **Significantly Improves circulation** (via vasodilation)
- **Reduces inflammation**
- **Decreases pain**
- **Increases angiogenesis**
  - Builds new vessels
- **Increases lymphatic activity**
  - Decreases swelling

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NO Release From Tissue or Blood:

- **Increases cell regeneration** (wound healing)
  - Stimulates tissue granulation & connective tissue
- **Increases bone mineralization**
  - Reduces osteoporosis
- **Increases phagocytosis** (immune response)
- **Increases RNA-DNA synthesis** (cell building)
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• Certain vegetables possess a high nitrate content representing a potential source of vasoprotective nitric oxide via bioactivation.

• In healthy volunteers, approximately 3 hours after ingestion of a dietary nitrate load (beetroot juice 500 mL), BP was substantially reduced (max 10.4/8 mm Hg); an effect that correlated with peak increases in plasma nitrite concentration.

Abstract—Diet rich in fruits and vegetables reduce blood pressure (BP) and the risk of adverse cardiovascular events. However, the mechanisms of this effect have not been elucidated. Certain vegetables possess a high nitrate content, and we hypothesized that this might represent a source of vasoprotective nitric oxide via bioactivation. In healthy volunteers, approximately 3 hours after ingestion of a dietary nitrate load (beetroot juice 500 mL), BP was substantially reduced (ΔBP = −10.4/8 mm Hg); an effect that correlated with peak increases in plasma nitrite concentration. The dietary nitrate load also prevented endothelial dysfunction induced by an acute ischemic insult in the human forearm and significantly attenuated ex vivo platelet aggregation in response to collagen and ADP. Interruption of the enterosalivary conversion of nitrate to nitrite (facilitated by bacterial anaerobes situated on the surface of the tongue) prevented the rise in plasma nitrite, blocked the decrease in BP, and abolished the inhibitory effects on platelet aggregation, confirming that these vasoprotective effects were attributable to the activity of nitrite converted from the ingested nitrate. These findings suggest that dietary nitrate underlies the beneficial effects of a vegetable-rich diet and highlights the potential of a “natural” low cost approach for the treatment of cardiovascular disease.

Key Words: diet • nitrate • blood pressure • hypertension • ischemia/hypertension • platelets • endothelium

Perhaps the largest public health initiative in the Western world has focused on improvement of diet, particularly in those with a high risk of cardiovascular disease. Trials have shown that diets rich in fruits and vegetables reduce blood pressure (BP, Dietary Approaches to Stop Hypertension; DASH, Vegetarian Diet and BP+) and adverse cardiovascular events. These protective effects have previously been attributed to the high antioxidant vitamin content, yet large clinical trials have failed to provide evidence in support of this thesis. The greatest protection against coronary heart disease afforded by a change in diet is associated with the consumption of green leafy vegetables (eg, spinach, lettuce). Such vegetables, also including beetroot, commonly have a high inorganic nitrate (NO\textsubscript{3}−) content. In humans, after absorption through the stomach wall, ~75% of consumed nitrate enters the enterosalivary circulation where it is reduced to nitrite (NO\textsubscript{2}−) by bacterial nitrate reductases from facultative anaerobes on the dental surface of the tongue. This nitrite is swallowed and in the acidic environment of the stomach is reduced to nitric oxide (NO) or re-enters the circulation as nitrite. Indeed, it has been hypothesized that dietary nitrate represents an intravascular source of the pleiotropic, vasoprotective molecule NO, which supplements conventional NO generation by NO synthases (NOS).–

Endothelium-derived NO is a potent dilator, governs systemic BP, and retards atherosclerosis (NO inhibits inflammatory cell recruitment and platelet aggregation). Consequently, numerous cardiovascular pathologies (including prehypertension, hypertension, atherosclerosis, and stroke) are associated with endothelial dysfunction and diminished NO bioactivity. Recently, studies have demonstrated that nitrite could mediate protection against ischemia/reperfusion (I/R) injury in the myocardial, hepatic, renal, pulmonary, and cerebral vasculature. This cytoprotective effect has been attributed to reduction of nitric oxide (NO) during ischemia or hypoxia (conditions that inactivate endothelial NOS, the...
Figure 1. The effect of beetroot juice on the plasma concentrations of (a) nitrate and (b) nitrite and the effects of spitting vs swallowing of saliva on plasma concentrations of (c) nitrate and (d) nitrite.
### Classification of vegetables according to nitrate content

<table>
<thead>
<tr>
<th>Nitrate content (mg/100 g fresh weight)</th>
<th>Vegetable varieties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low, &lt;20</td>
<td>Artichoke, asparagus, broad bean, eggplant, garlic, onion, green bean, mushroom, pea, pepper, potato, summer squash, sweet potato, tomato, watermelon</td>
</tr>
<tr>
<td>Low, 20 to &lt;50</td>
<td>Broccoli, carrot, cauliflower, cucumber, pumpkin, chicory</td>
</tr>
<tr>
<td>Middle, 50 to &lt;100</td>
<td>Cabbage, dill, turnip, savoy cabbage</td>
</tr>
<tr>
<td>High, 100 to &lt;250</td>
<td>Celeriac, Chinese cabbage, endive, fennel, kohlrabi, leek, parsley</td>
</tr>
<tr>
<td>Very high, &gt;250</td>
<td>Celery, cress, chervil, lettuce, red beetroot, spinach, rocket (rucola)</td>
</tr>
</tbody>
</table>
Nitrite levels in cells treated with L-citrulline and GSH were significantly greater than control ($p < 0.05$).

Plasma NOx with L-citrulline + GSH was significantly greater than control and L-citrulline ($p < 0.05$).

Nitrite and NOx for L-citrulline + GSH were significantly greater at 30 min post-exercise when compared to placebo ($p < 0.05$).

**Conclusion:**
Combining L-citrulline with GSH augments increases in nitrite and NOx levels during *in vitro* and *in vivo* conditions.

Nitric Oxide (NO)

890nm IR

IR

RBC

Endothelial Cell

Dietary / Nutritional Nitrate / Nitrite Present In Circulation

890nm IR is absorbed by hemoglobin and endothelial cells

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Nitric Oxide (NO)
Forty-nine subjects with established diabetic peripheral neuropathy were treated with monochromatic near-infrared photo energy (MIRE) to determine if there was an improvement of sensation.

Loss of protective sensation characterized by Semmes-Weinstein monofilament values of 4.56 and above was present in 100% of subjects (range, 4.56 to 6.45), and 42 subjects (86%) had Semmes-Weinstein values of 5.07 or higher.
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Figure 1. Percentage distribution of patients with type 1 diabetes (N = 25) with Semmes-Weinstein monofilament values ≥ 5.07 and ≤ 4.93 before (left) and after (right) 12 MIRE treatments.

Figure 2. Percentage distribution of patients with type 2 diabetes (N = 24) with Semmes-Weinstein monofilament values ≥ 5.07 and ≤ 4.93 before (left) and after (right) 12 MIRE treatments.
The ability to discriminate between hot and cold sensation was absent (54%) or impaired (46%) in both groups prior to the initiation of MIRE treatment. 48 subjects (98%) exhibited improved sensation after 6 treatments, and all subjects had improved sensation after 12 treatments. Therefore, MIRE may be a safe, drug-free, noninvasive treatment for the consistent and predictable improvement of sensation in diabetic patients with peripheral neuropathy of the feet. (J Am Podiatr Med Assoc 92(3): 125-130, 2002)
27 patients with peripheral neuropathy received treatment with monochromatic near-infrared photoenergy (890 nm).

Methods: All enrolled patients exhibited abnormal sensory perception (either hyperesthesia or hypoesthesia) based on a qualifying examination with the Neurometer CPT (current perception threshold) (baseline CPT). The patients received 10 treatments (each lasting 40 minutes) during a 2-week period and then underwent CPT retesting to determine the extent of improvement of sensory impairment in myelinated and unmyelinated sensory fibers of the peroneal nerve.
Results: All patients obtained improvement in sensory impairment in comparison with baseline CPT measures, and 16 of the 27 patients achieved normal sensory responses in all nerve fiber subpopulations. Ten patients had been tested previously (initial CPT) and did not exhibit spontaneous improvement in sensory impairment during a mean period of 27 months before baseline CPT. After receiving the ATS treatments, however, this group of patients showed improvement in comparison with both initial CPT results and baseline CPT.

Conclusion: On the basis of the data from this study, the ATS seems to be a safe and effective treatment to improve sensory impairment associated with peripheral neuropathy due to diabetes and other causes. *(Endocr Pract. 2004;10:24-30)*
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Diagram of the various medical applications of low-level light therapy.
THANK YOU!

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