Photodynamic Therapy and Photobiomodulation

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Introduction

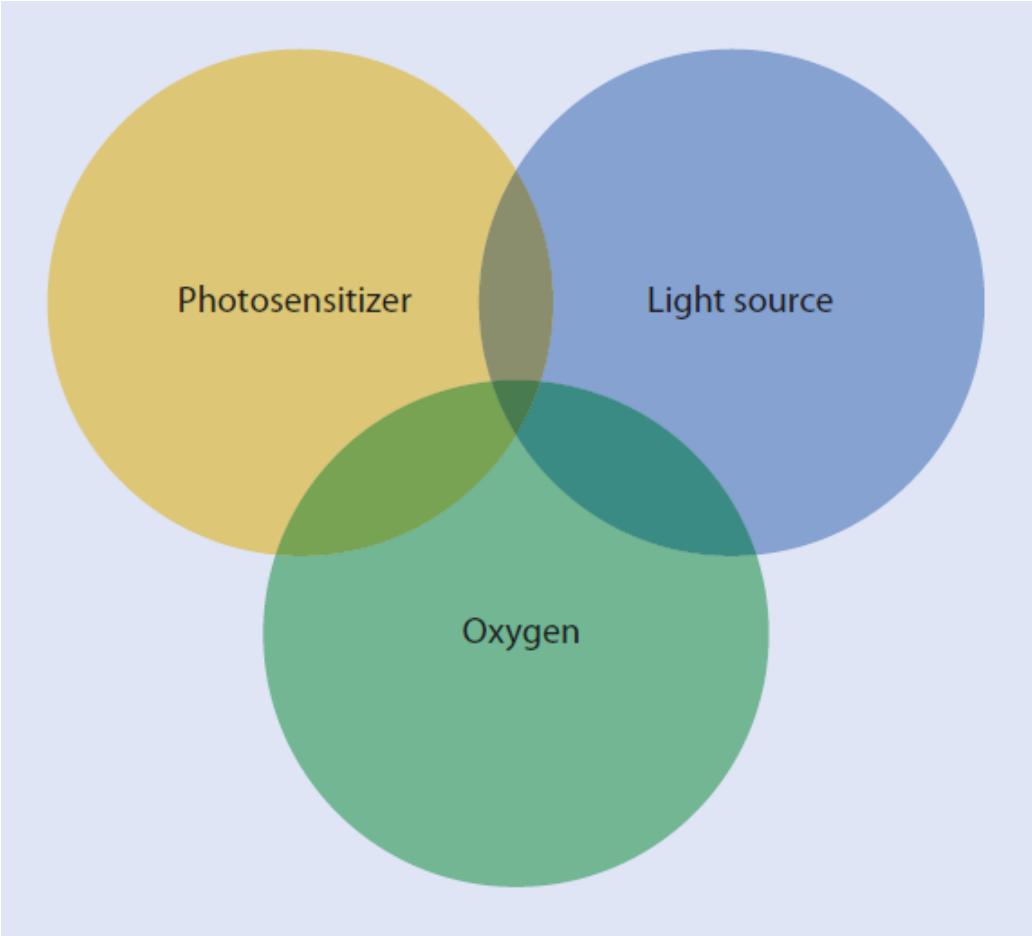
- Laser is used for many therapeutic applications to treat different diseases.
- In this lecture, We will talk about two types of modalities or techniques that use particular types of lasers to treat several types of cases
- These techniques are

1- Photodynamic Therapy

2- Photobiomodulation Therapy

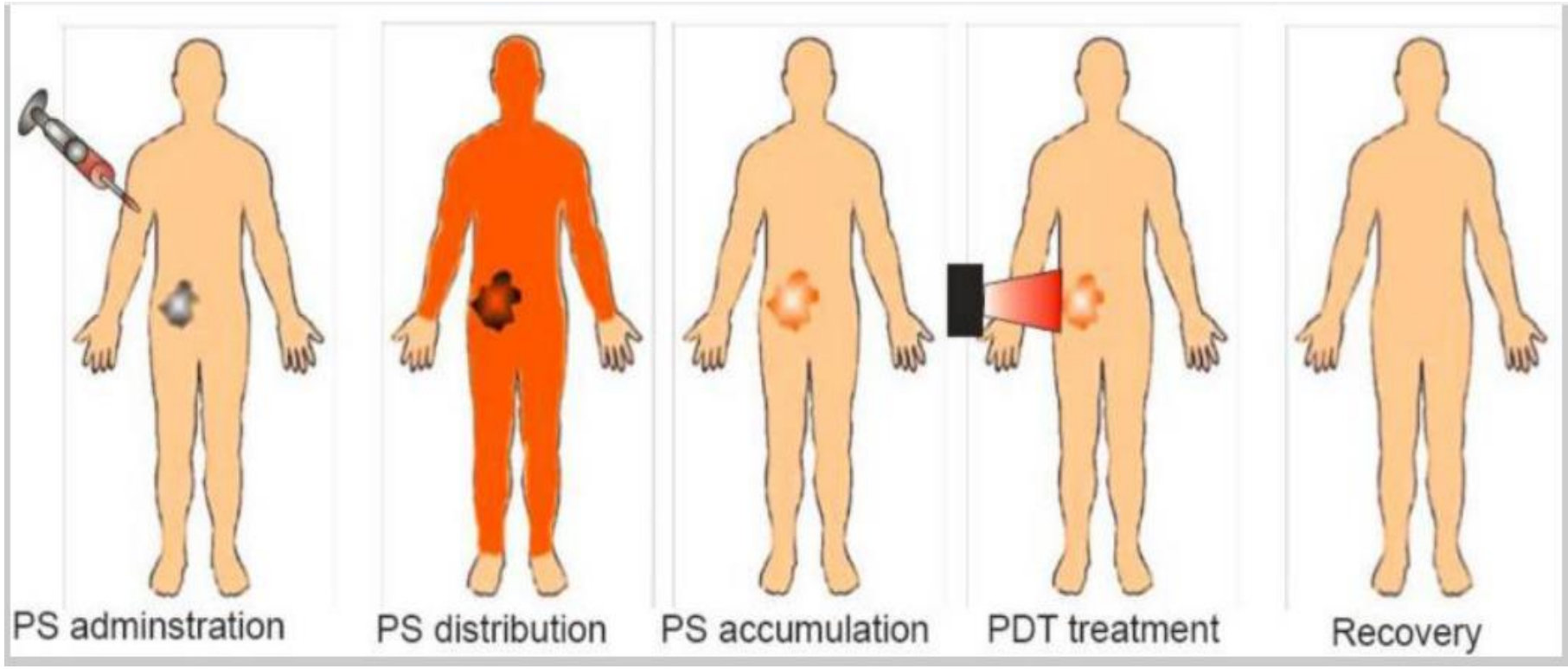
1- Photodynamic Therapy (PDT)

- Photodynamic therapy (PDT) is a treatment that uses a drug which is called a photosensitizer (light-activated drug), and a particular type of light (usually laser) to destroy cancerous and precancerous cells.
- An activation of photosensitizer(PS)drugs with specific wavelengths of light leads to energy transfer to the molecules in the surrounding areas, generating **cytotoxic reactive oxygen species(ROS**) which can trigger cell death
- The photosensitizer is nontoxic until it is activated by light. However, after light activation, the photosensitizer becomes toxic to the targeted tissue.
- The successful outcome of PDT critically depends on three elements: photosensitizer, light source, and oxygen



The three basic elements of PDT

Steps of PDT to treat cancer



Steps of PDT to treat cancer

- 1- A photosensitizer drug is given to the patient depending on the area of the body that's being treated. The photosensitizer may be a cream, injection, or special drink.
- 2- The photosensitizer is absorbed by cells all over the body but stays in cancer cells longer than it does in normal cells.
- 3- Approximately 24 to 72 hours after giving the photosensitizer, when most of the drug has left normal cells but remains in cancer cells, the tumor is exposed to light (Laser).
- 4- The photosensitizer in the tumor absorbs the Laser and produces toxic products that destroy nearby cancer cells

Photosensitizer (PS)

- A photosensitizer is a chemical compound, which, when activated by an appropriate wavelength, forms a highly reactive oxygen species which results in cell death.
- **Characteristics of photosensitizers**
- 1- Absorption spectrum (have activation at a specific wavelength)
- 2- Photoactivity
- 3- Pharmacokinetics (how distribute in the body)
- 4- Microlocalization in the tumor
- **These 4 factors determine the PDT efficacy**

- **Other characteristics of photosensitizers**
- 1- Delivery vehicle (some drugs need delivery vehicle)
- 2- Toxicity (the drug should not be toxic in the dark, before activation by light)
- 3- Phototoxicity (the drug should be toxic after activation by light, and possess the ability to produce a huge amount of cytotoxic products after activation by light)
- 4- Be rapidly eliminated from normal tissue
- 5-Photostability
- 6- Cost (economical and easily available)

Light Source

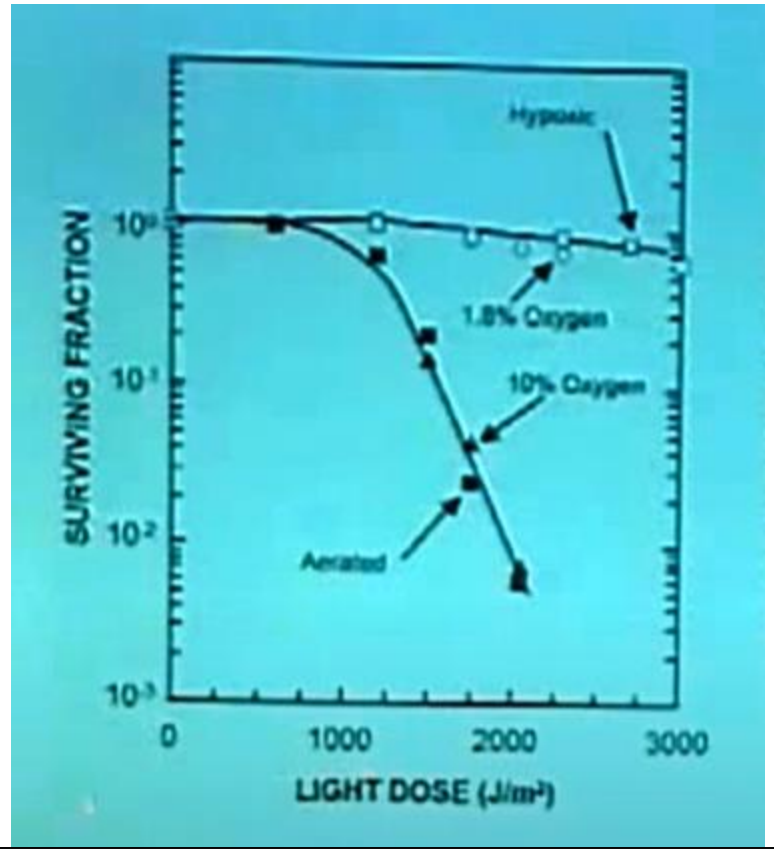
- The choice of light source depends on
- 1-Target location (optimal tissue penetration for lesion depth/volume)
- 2- Photosensitizer used (The wavelength of the light source must be matched by the absorption wavelength of the photosensitizer)
- 3- Light dose to be delivered
- To get maximum penetration, red light or infrared are used
- To treat tumor located 1-2 cm deep, long wavelengths are used such as red or infrared
- The light source for PDT can be classified into three types:
- 1. Broad-spectrum lamps
- 2. Light-emitting diode lamps (LED)
- 3. Lasers such as Argon Lasers, Argon-pumped Dye Lasers, Nd: YAG lasers, and Diode Lasers
- At present, diode lasers are the most common light sources for clinical PDT.

Light Source (Laser)

- Lasers are widely used for superficial and interstitial PDT.
- Unique properties of lasers are that the laser generates a monochromatic light, with a very narrow bandwidth, and is coherent.
- Lasers provide high optical power and a wavelength that can be controlled to correspond to a specific photosensitizer.
- For treatment of superficial lesions: In order to cover a relatively large target tissue with uniform irradiance, the laser can be coupled with beam-expanding lenses.

Oxygen presence

- The presence of oxygen in tissues is important for PDT
- PDT need adequate tissue oxygenation
- At a low level of oxygen, the efficiency of PDT will be less



In vitro, tumor cells survival curves, (using the same drug and same light source, but the difference was in oxygen level)

Sub- Cellular and molecular targets of PDT

- Destructions induced by PDT
  - cell membrane
  - Cytoplasm
  - Nucleus
  - Mitochondria
  - Lysosomes
  - Golgi
  - Lipids

- Photosensitizers accumulate in the cytoplasm(outside the nucleus), therefore, PDT doesn't damage the DNA which is located inside the nucleus

Advantages of PDT

- It has no long-term side effects when used properly.
- It’s less invasive than surgery.
- It usually takes only a short time and is most often done as an outpatient procedure.
- It can be targeted very precisely.
- Unlike radiation, PDT can be repeated many times at the same site if needed.
- PDT mostly targets mitochondria while radiation therapy and chemotherapy target DNA. Therefore, PDT procedure can be used to treat all types of cancer cells
- There’s usually little or no scarring after the site heals.
- It often costs less than other cancer treatments.

Limitations of PDT

- PDT can only treat areas where light can reach. This means it's mainly used to treat problems on or just under the skin, or in the lining of organs that can be reached with a light source. Because light can't travel very far through body tissues, PDT can't be used to treat large cancers or cancers that have grown deeply into the skin or other organs.
- PDT can't be used to treat cancers that have spread to many places.
- The drugs used for PDT leave people very sensitive to light for some time, so special precautions must be taken after the drugs are put in or on the body.
- PDT can't be used in people who have certain blood diseases.

2- Photobiomodulation Therapy(PBMT)

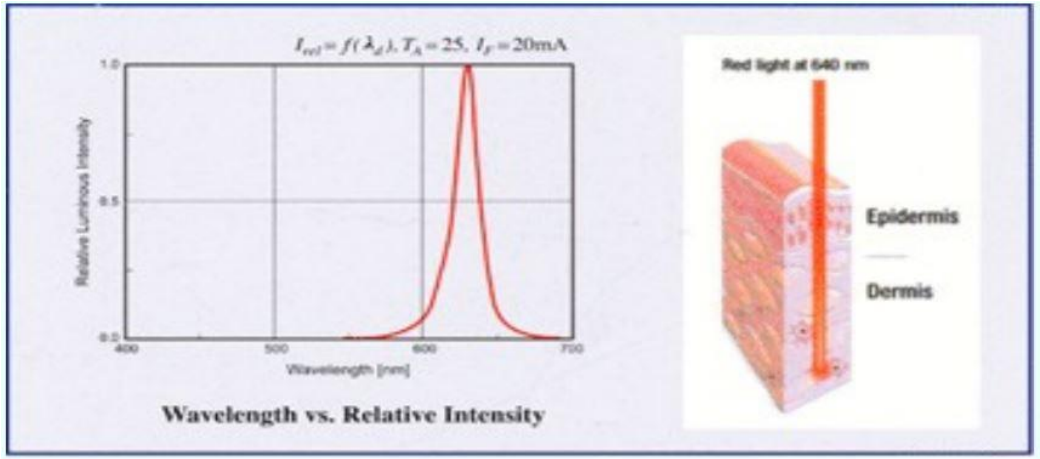
- Photobiomodulation (PBMT) is a form of medicine that applies low-level lasers or light-emitting diodes to the surface of the body (pathological tissue)to stimulate, heal, regenerate, and protect tissue that has either been injured, is degenerating, or is at risk of dying.
- Photobiomodulation was previously called Low-level laser therapy (LLLT)
- Why we prefer LASER in Photobiomodulation?

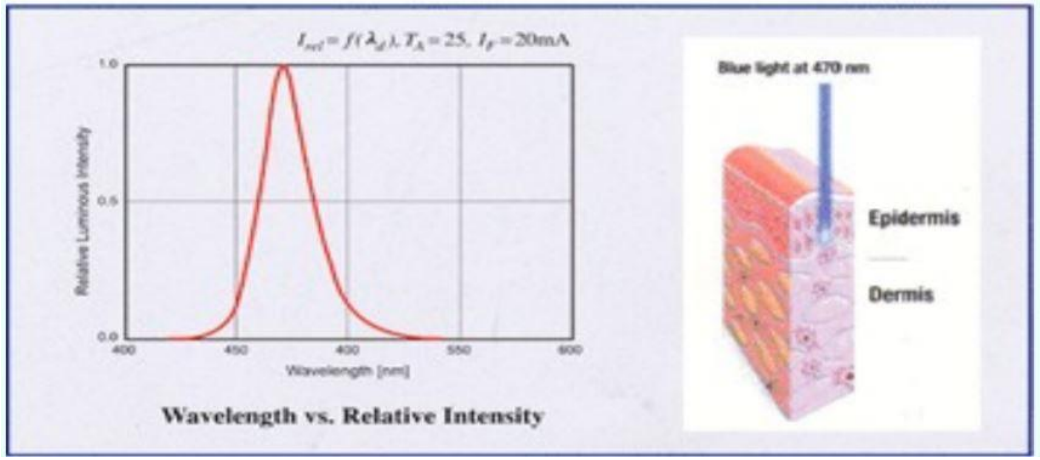
Because it is a well-defined source of light that is almost monochromatic, polarized, coherent, can be precisely dosed in intensity and studied regarding its biological effects

Why the wavelength of red or near-infrared is preferred In Photobiomodulation Therapy?

Because this range of wavelength can penetrate the skin and can reach other tissues while the blue light stops at the first layer of the skin

Greater Wavelength = Deeper Penetration





Mechanism of Photobiomodulation Therapy

- When lasers illuminate biological tissues, energy is delivered to the living system and must be absorbed for effective results

- Photobiomodulation works mostly through non-thermal photobiological mechanisms where laser (visible and near-infrared radiation) is absorbed in the respiratory chain molecules in the mitochondria (e.g., cytochrome c oxidase), which results in increased metabolism, which leads to signal transduction to other parts of the cell, including cell membranes, and ultimately to the photoresponse (e.g., stimulation of growth).

- Mitochondria are thought to be the main site for the initial effects of light and specifically cytochrome c oxidase that has absorption peaks in the red and near infrared regions of the electromagnetic spectrum matches the action spectra of Photobiomodulation effects

- The process of absorption is relevant to laser parameters, such as wavelength and output power, as well as factors of the biological tissue (anatomy, physiology, pathology, and tissue optics). Laser fluence, or energy density (ED), is still considered to be the most an important variable in laser therapy

Mechanism of Photobiomodulation Therapy

- Although the primary mechanisms of are not completely understood, in vitro and in vivo studies suggest that Photobiomodulation
- 1- Increases cellular proliferation.
- 2- Increases uptake of ATP
- 3- Increases cell membrane permeability to Ca2+
- 4- Regulates growth factors and cytokines (cytokines are a large group of proteins, peptides, or glycoproteins that are secreted by specific cells of the immune system)
- 5-Stimulates cellular differentiation and proliferation
- 6- Induces synthesis and remodeling of collagen,

Mechanism of Photobiomodulation Therapy

- This sum of these cellular events stimulated by Photobiomodulation restores homeostasis in injured tissues (normalization of their shape and function) leading to repair.

- Physiological Effects of Photobiomodulation are

1- Acceleration of tissue healing

2- Increased circulation

3- Pain reduction

4- Decreased Inflammation

(a)

(b)

(a) Healing of a surgical incision (sternotomy) post cardiovascular surgery following Photobiomodulation therapy .
(b) Conventional inpatient treatment of a surgical incision in another patient.

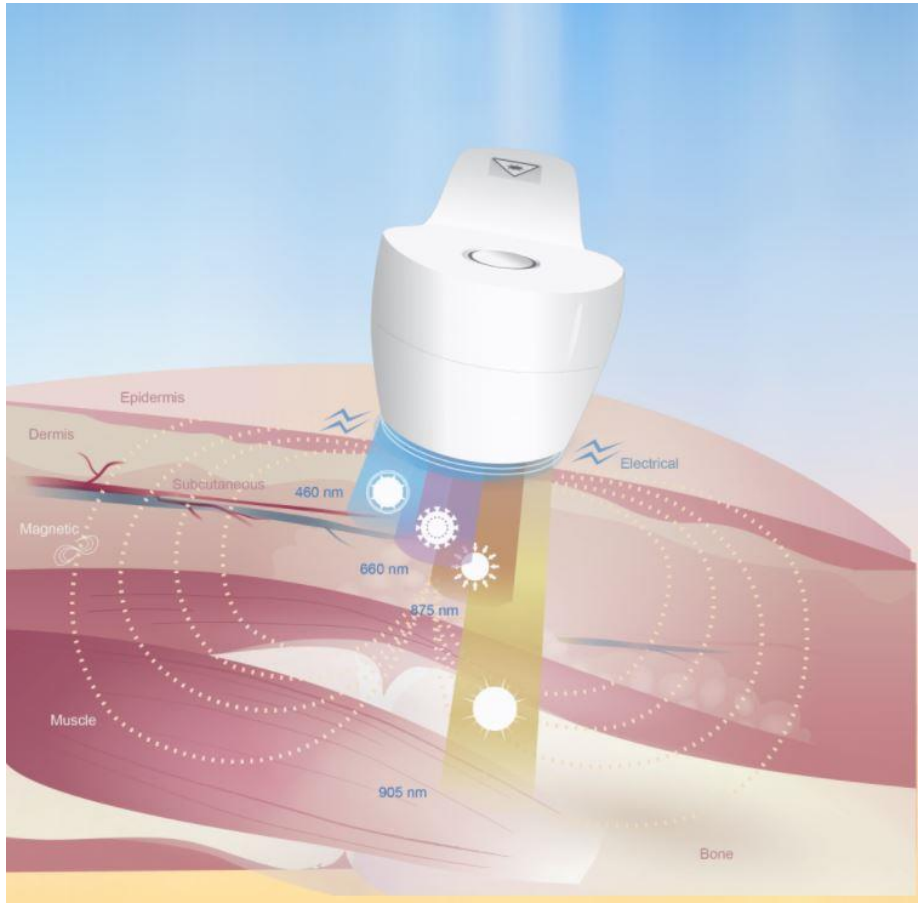
Types of Devices Used in the Delivery of Photobiomodulation Therapy

1 - Super Pulsed Laser Diode

a) Power = 15 W

b) Wavelength = 905 nm

c) Penetration (10—13 cm)



Types of Devices Used in the Delivery of Light Therapy

2- 4 Infrared LED's

a) Power = 60 mW

b) Wavelength = 875 nm

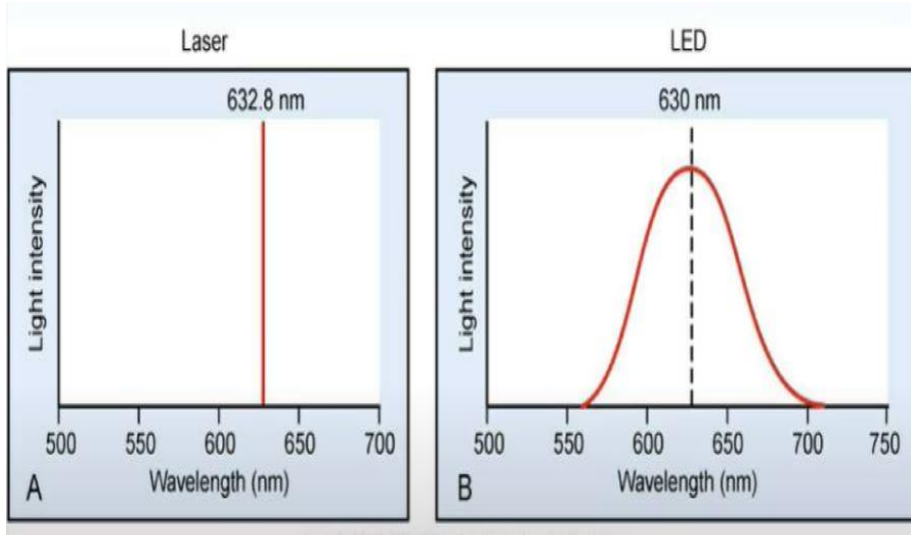
c) Medium and Broad Penetration

3- 4 Red LED's

a) Power = 7.5 mW

b) Wavelength = 660 nm

c) Shallow and Broad Penetration



Advantages of Photobiomodulation Therapy

- It induces a complex chain of physiological reactions in diseased and damaged tissues to
- 1- accelerate wound healing and tissue regeneration,
- 2- increase circulation,
- 3- reduce acute inflammation,
- 4- reduce acute and chronic pain
- 5- help restore normal cellular function.

Contraindications

PBMT can not be used if

1- cancer
2- Within 4 to 6 months after radiotherapy
3- Direct irradiation of the eyes
4- Photophobia or abnormally high sensitivity to light
5- When using photosensitizing medication
6- Direct irradiation over the fetus or the uterus during pregnancy
7- Direct irradiation over the thyroid gland or other endocrine glands
8- Over hemorrhaging lesions


Thank You
For Your
Attention