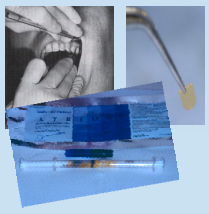
Review of Photodynamic Therapy of Periodontal Diseases

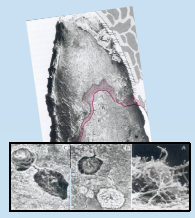
Dr. Hayder Al-Waeli
Jordan University of Science & Technology

Introduction



Periodontal diseases is one of the major causes of tooth loss in adults* and is considered primarily an anaerobic bacterial infection caused by the so called red complex species. Bacteria present in a biofilm community, Enzymes, endotoxins, and other cytotoxic factors from these bacteria lead to tissue destruction and initiate chronic inflammation.

The current treatment regimen involves mechanical debridement and this may be augmented with antibiotic therapy. Antimicrobial agents used systemically or as a local drug delivery further suppress the periodontal pathogens increasing the benefits of conventional mechanical therapy. However, the emergence of resistant microorganisms and a shift in the microflora after extended use, limits the use of antimicrobials. Other approaches to the local delivery of antimicrobial agents were investigated, including the use of photodynamic therapy (PDT). Since the 1890s, scientists used the staining properties of dyes to develop the idea of selective toxicity. This created the foundation for our modern use of chemotherapy. The application of light and dyes to destroy microbial species in vitro has been reported for many years.



Photodynamic Therapy

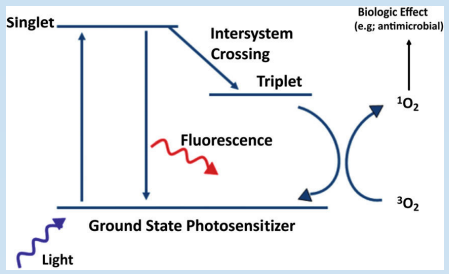
It is the light induced non-theramic inactivation of cells, microorganisms or molecules.

Light Sources

- A laser or visible light source is used to activate the photosensitizer.
- Diod laser system & light-emitting diods are used.
- Photosensitizers can also be activated by low power visible light at a specific wavelength.
- Light must penetrate as far as possible into the tissues and not produce thermal effects.

Light Sources Now

- Wave-length matched to photosensitizer
- Safe & non-damage to host tissue
- Portable
- Non-thermal diod laser
- Advanced fiberoptics

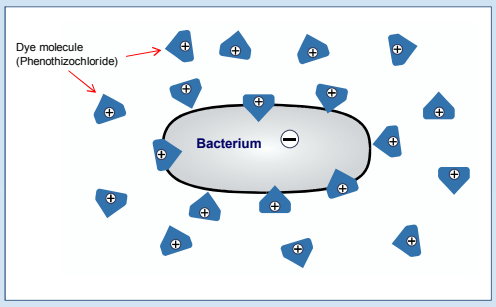


Photosensitizer in Periodontal Therapy

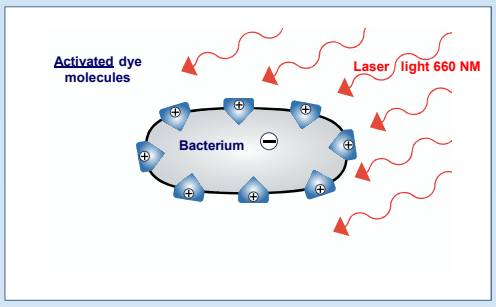
- Ideally should be: non-toxic & activated upon illumination
- Should bind with bacteria & plaque without causing any cosmetic issues, such as unwanted staining of gingiva & other soft tissues
- Easily access pathogens present in deeper periodontal pockets

- Dyes: 1-Tricyclic dyes (methylene blue, toludine blue O & acridine orange) 2-Phthalocyanines (aluminum disulphonated phthalocyanine and cationic Zn(II) phthalocyanine)
- Chlorines: chlorine e6, stannous (IV) chlorine e6, chlorine e6-2.5 N-methyl-d-glucamine (BLC1010), polylysine & polyethyleneimine conjugates of chlorine e6
- Porphyrines: haematoporphyrin HCl, photofrin and 5- minolevulinic acid (ALA), benzoporphyrin derivative (BPD)
- Xanthenes: Erythrocine
- Monoterpene: azulene

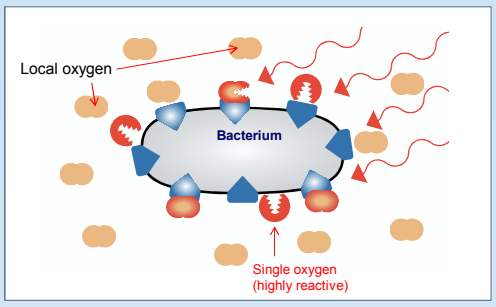
1. Dye molecules adapt to the bacteria membrane



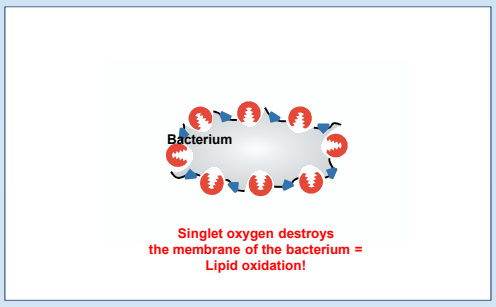
2. Laser light activates dye molecules

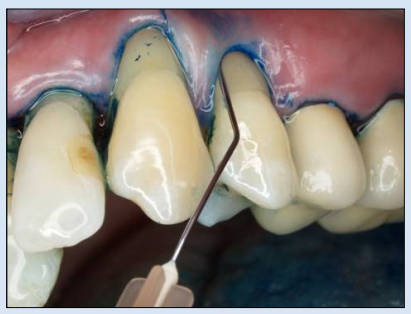


3. Reaction with oxygen leads to the building of singlet oxygen

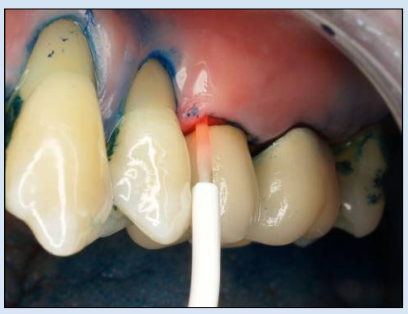


4. Aggressive singlet oxygen oxidates the membrane of the bacterium

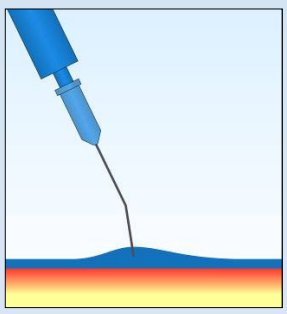




Application of **HELBO®*Blue Photosensitizer:*** **Important:** to apply the dye solution from apical to coronal direction!

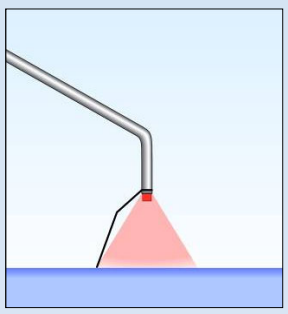


Light exposuring / HELBO®*TheraLite Laser* ⇒ **1 min per tooth** ⇒ **killing of bacteria**



Application of **HELBO®*Blue Photosensitizer,*** staining of the microorganisms: ⇒ **Reaction time 3 min**

Before exposure with the **HELBO®*TheraLite Laser*** ⇒ **Rinse with H_2O!**



Surface exposure with the **HELBO®*TheraLite Laser*** ⇒ **min. 1 min per cm² = 30 sec. per area**

Studies on PDT of Periodontal Diseases

PDT on plaque biofilm in *in vitro* studies

Photosensitizer	Light (nm*)/laser source	Periodontal pathogens
Toludine blue O Methylene blue Aluminum disulphonated phthalocyanine	633 nm Helium/Neon	Streptococcus sanguinis Porphyromonas gingivalis Fusobacterium nucleatum Actinomyces actinomycetemcomitans
Hematoporphyrin HCl[23] Aluminum disulphonated phthalocyanine[24] Chlorine e6-pentalysin conjugate[25] Toluidine blue[26]	660 LED¶ Red light (662)	Streptococcus sanguinis A. actinomycetemcomitans Fusobacterium. nucleatum, Porphyromonas gingivalis, Campylobacter rectus, Eikenella corrodens Streptococcus sanguis
Toludine blue O (25 um)[27] Porphycene–Polylysine Conjugates (10 μm**)[28]	Red light (4.4 J) Visible light	Porphyromonas gingivalis Prevotella intermedia, Fusobacterium nucleatum, Peptostreptococcus micros Actinobacillus actinomycetemcomitans
Methylene blue[29]	665 nm Diode laser	A. actinomycetemcomitans, Fusobacterium nucleatum, Porphyromonas gingivalis, Prevotella intermedia, Streptococcus sanguis
Toluidine blue O (12.5 μg/ml)[30]	Helium–Neon red-filtered Xenon lamp	Porphyromonas gingivalis
5-aminolevulinic acid[31] Poly-L-lysine–chlorin e6 conjugates[32] Chlorine e6, BLC 1010, BLC 1014[33]	630 LED Red light diode (671) Diode (662)	Pseudomonas aeruginosa Actinomyces viscosus Porphyromonas gingivalis Fusobacterium nucleatum, Porphyromonas gingivalis, Capnocytophaga gingivalis
Endogenous porphyrins[34]	Blue light (380 to 520)	Prevotella intermedia, P. nigrescens, P. melaninogenica, P. gingivalis
Toludine blue O (1 mg/ml)[35]	Diode laser (635), 12 J/cm²	Leptotrichia buccalis, Vignal's bacillus, Fusobacterium, Actinomycetes, Chain coccus Streptococcus, Veillonella, etc.

¶Light-emitting diodes.
*nm = nanometer.
** = micromolar concentration.
J = Joules.

Various ***in-vitro*** studies have shown that periodontal micro-organisms are killed more than 4–5 times at micromolar concentration after incubation times as short as 5–10 minutes and irradiation under mild experimental conditions, such as fluence rates around 50 mW/cm² and irradiation times shorter than 15 minutes

PDT in *in vivo* studies

Citation	Population and Location	Mean Age (years [range] or [± SD])	Female/Male Ratio	Periodontal Status	Method	Photosensitizer	Laser	Wave-Length (nm)	Maximum Power (mW)	Irradiation Time
de Oliveira et al., 2007[24]	10 patients with a total of 10 pairs of contralateral maxillary single-rooted teeth; PD ≥5 mm on at least two aspects of a tooth; Ribeirão Preto, São Paulo, Brazil	31	2/8	Aggressive periodontitis	Supragingival tooth cleaning 7 days before baseline: PDT alone in one tooth/pair; SRP alone with hand instruments for another tooth/pair	Phenothiazine chloride in a concentration of 10 mg/ml*	Diode laser*	660	60	10 seconds per site for six sites per tooth, a total of 1 minute
Andersen et al., 2007[25]	622 individual sites treated; subjects from Everett, Washington	53 (18 to 75)	22/11	Moderate to advanced periodontal disease	n = 33 in three study arms: group 1) PDT, n = first five patients; group 2) SRP, n = 14; group 3) both SRP + PDT, n = 14 (SRP was performed by one clinician)	Phenothiazine chloride†	Diode laser‡	670	150	1-minute irradiation time per site
Braun et al., 2008[26]	n = 20 patients; Bonn, Welschnonnenstrasse, Germany	46.6 (± 6.1)	11/9	Untreated chronic periodontitis						
Christodoulides et al., 2008[27]	24 subjects; Nijmegen, The Netherlands	45 (± 8.11)	13/11	Chronic periodontitis	n = 20; SRP for all teeth; split-mouth design: two quadrants: PDT	Phenothiazine chloride*	Diode laser*	660	100	10 seconds per site and six sites per tooth for a total of 1 minute
Yilmaz et al., 2002[28]	10 patients with four single-rooted teeth each (one/quadrant); PD >4 mm mesio-buccally; Istanbul, Turkey	NA	NA	Early to mild periodontitis	Baseline: 1) SRP; 2) SRP + PDT; 6-month follow-up: one session of prophylaxis, OHI, and supragingival debridement	Phenothiazine chloride§	Diode laser*	670	75	1 minute of irradiation
					Microbiologic (one site/tooth) and clinical assessment (six sites/tooth) n = 10; each dental quadrant randomly received one of four types of treatment procedures: SRP, PDT, PDT + SRP, or OHI	Methylene blue rinse‖	Gallium-arsenide diode laser¶	685	Frequency of 5.0 Hz and delivering a 30 mW with a power density of 1.6 J/cm²	1.11 minutes, three times per week, over each papillary region

OHI = oral hygiene instructions; PD = probing depth; NA = not available.
* HELBO Photodynamic Systems, Grieskirchen, Austria.
† Periowave Treatment Kit, Ondine Biopharma, Vancouver, BC.
‡ Periowave, Ondine Biopharma.
§ HELBO Blue Photosensitizer, HELBO Photodynamic Systems.
‖ Buco bleu 15 g, Sandoz, Istanbul, Turkey.
¶ BTL-2000, BTL, Prague, Czech Republic.

Clinical trials are also encouraging. In addition to reducing clinical parameters in peri-implantitis cases, there is some evidence that PDT will also inactivate virulence factors of periodontal pathogens, enhancing post-treatment outcomes.
Meta analysis for the available clinical trials, indicate that there are not yet enough data to show that PDT is efficacious*

Conclusions & Suggestions

- This new strategy of using PDT is less traumatic & quicker in the treatment of inflammatory periodontal diseases
- Photodynamic therapy in vitro studies have shown greater (> 95%) reduction in micro-organisms.
- PDT offers numerous advantages, particularly in avoiding emergence of antibiotic resistance species, requiring less technical skills & reducing operating time in comparison to manual scaling and root planing.
- Well-designed clinical trials are needed for proper evaluation of this therapy.
- Multi discipline clinical trials should be designed to establish the clinical evidance based effectivness of PDT in periodontal, endodontics and even orthodontic treatment.

References

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