pISSN 0898-5901 | eISSN 1884-7269
Indexed in Scopus

Volume 31 - N. 1

# Light-Emitting-Diode photochemical effects in dentistry: an overview

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## ABSTRACT

This work aims to show the important role that might be played by the daily utilization of LED technology in dentistry, as well as to suggest the advantages of the application of Light-Emitting-Diode (LED) Photobiomodulation (PBM) and PhotoDynamic Therapy (PDT) for the treatment of a large number of oral diseases. It presents an overview of the most recent and interesting studies on PBM and PDT by LED light in periodontics, endodontics, orthodontics, implantology, and Oral Medicine. LED light utilization offers several advantages compared to Laser: the possibility to treat large surfaces, low cost, and safety for patients and operators. The use of LED in dentistry may represent a great help for treating a large number of diseases with low costs and without side effects.

**Key words:** Light-Emitting-Diode, LED, photobiomodulation, PBM, photodynamic therapy, PDT, dentistry.

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Received: 13 November 2023.
Accepted: 19 January 2024.

*Laser Therapy*

Laser Therapy 2024; 31:377
doi:10.4081/ltj.2024.377

## Introduction

Andre Mester, in 1967, observing the improvement of the healing process in scare rats after low-power Ruby laser irradiation,[1] proposed the utilization of this procedure in medicine and started to successfully treat non-healing and difficult-healing human skin and mucosal ulcers and wounds.[2]
Subsequently, many Authors studied in detail the mechanisms of action of low-energy laser irradiation in the tissues.
Karu indicated mitochondria as the most cellular component sensitive to visible and near IR radiations,[3] and Hamblin *et al.*, confirming this theory, suggested as the final result the increasing of adenosine triphosphate (ATP) production, deoxyribonucleic acid (DNA) synthesis, reactive oxygen species (ROS) and nitric oxygen species (NOS) modulation and transcription factors induction.[4]
Moreover, Kulbacka et al. demonstrated that visible wavelengths, mainly blue and green, are also active in intracellular Calcium increase.[5]
Low-power laser irradiation has now developed into a therapeutic procedure that is used in three main ways: to reduce inflammation, edema, and chronic joint disorders, to promote the healing of wounds, deeper tissues, and nerves, and to treat neurological diseases and pain.[6]
In 2019, Juanita Anders *et al.*, to avoid confusion about the terminology that time adopted (LLLT, soft laser, cold laser, biostimulation, and so on), proposed only to use the term Photobiomodulation (PBM), so enhancing also that, by this technique, is possible to make both stimulation and inhibition.
At the same time, she affirmed that Laser and Light-Emitting-Diode (LED), at low power, have the same kind of effects in the biological tissues.[7]
This was confirmed in 2018 by Heiskanen and Hamblin who enhanced the advantages of LED light in PBM including no laser safety considerations, ease of home use, ability to irradiate a large area of tissue at once, possibility of wearable devices, and much lower cost per mW.[8]
PhotoDynamic Therapy (PDT) uses the association of particular agents called photosensitizers (PS) and visible or near-infrared light, with a wavelength specific for each PS irradiation. Even if both light and PS are non-toxic alone, their association starts a photochemical reaction: the final result is the Reactive Oxygen Singlet (ROS),[9] able to destroy biological targets such as cancer cells and microbes, including bacteria.[10]
The capability of PDT to selectively kill several kinds of micro-organisms was demonstrated by Merigo et al. in three different *in-vitro* studies,[11-13] and de Sousa and Al in 2010 showed by an *ex-vivo* investigation on 16 young male Wistar rats that the use of red and green LED light is effective on fibroblastic proliferation increasing.[14]
Enwemeka, in 2013, proposed to consider blue light as an alternative to antibiotics based on its high antibacterial power,[15] and Zupin *et al.*, in 2021, established that blue PBM LED therapy impacts SARS-CoV-2 by limiting its replication in Vero cells.[16]
LED technology has been used in dentistry for a long time: it was first introduced for the photopolymerization of composite resin[17] and subsequently to increase the bleaching effect of $H_2O_2$ with a low-temperature increase;[18] moreover, today, there is still a small number of clinical publications about the use of LED in dental PBM and PDT.
This work aims to show, by an overview of the most recent and interesting studies on this field, the important role that might be played by the daily utilization of LED technology in dentistry, as well as to describe the advantages of the application of LED PDT and PBM for the treatment of a large number of oral diseases.

## Materials and Methods

### ***Photobiomodulation***

#### *Orthodontics*

Orthodontics is one of the dental fields where most of the scientific papers regarding the use of LED PBMT were published.
De Fonseca *et al.*, in 2013, in a randomized, double-blind, placebo-controlled clinical trial involving 72 participants, evaluated the PBM effects on pain, edema, paresthesia, and bone regeneration after surgically-assisted Rapid Maxillary Expansion. They used two LED wavelengths (660 and 850 nm) both extraorally and intraorally, and they concluded that, due to maxillary disjunction surgeries reaching large anatomical areas involving intra and extraoral structures, LED sources can reach larger sites in the same application also combining different wavelengths that are absorbed by superficial and deeper tissues.[19]

The same conclusion was reached in 2014 by Rosa *et al.* with a Raman spectroscopy analysis, indicating that Laser and LED light irradiation improves hydroxyapatite deposition in the mid-palatal suture after orthopedic expansion.[20]
Caccianiga *et al.*, in 2021, investigated by a randomized clinical trial on 30 patients the effect of a LED with a combination of wavelengths from 450 to 835 nm on Pain Reduction during Rapid Palatal Expansion (RPE), and they concluded that PBM is efficient in reducing the intensity and the time of pain felt by young patients that undergo RPE.[21]
Ekizer *et al.*, in 2013, by an *in vivo* study performed on 20 male Wistar rats irradiated for ten days by a 618 nm LED lamp after five days of expansion, showed bone architecture improvement by histo-morphometric evaluation.[22]
The same Authors, in different works, demonstrated that LED-mediated-PBM therapy increases the accelerating orthodontic tooth movement at the same time while reducing the effects on orthodontically induced resorptive activity[23] and also plays a favorable role in healing and attachment of titanium orthodontic mini-screws.[24]
Shaughnessy *et al.*, in 2016, conducted an *in vivo* study on 19 subjects by testing the intraoral LED device effects on teeth movement during orthodontic treatment.
This device (OrthoPulse™, Biolux Research Ltd.) consists of near-infrared light with a continuous 850-nm wavelength, generating an average daily energy density of 9.5 J/cm$^2$.
It was applied daily to the test group patients, and the results demonstrated that intraoral PBM increased the average rate of tooth movement by 2.9-fold, resulting in a 54 % average decrease in alignment duration *versus* the control group.[25]
Levrini *et al.*, in 2022, performed a retrospective study on 376 patients treated with Invisalign® clear aligners in association with OrthoPulse® prescribed for 10 min a day for the entire duration of the orthodontic treatment and results showed that in the treated group the average number of additional aligners represented 66.5% of the initial aligners. In contrast, 103.4% of the initially planned aligners were needed in the control group.
They concluded that in patients treated with clear aligners, OrthoPulse® would increase the predictability of orthodontic treatment with clear aligners, thus reducing the number of finishing phase requirements.[26]
Guray *et al.*, in 2023, in a randomized controlled clinical trial on 30 patients with fixed orthodontic appliance irradiated with OrthoPulse™, concluded that this LED device may accelerate orthodontic tooth movement by 33%.[27]
LED PBM can also be significant in treating temporomandibular joint diseases (TMJD).
Costa *et al.*, in 2021, compared the effects of infrared LED therapy associated with an occlusal splint (OS) on the signs and symptoms of TMJD. Through their randomized, double-blind clinical trial on 70 patients, they concluded that the association of LED therapy and OS presented superior results concerning the isolated therapies, especially the protocol with two weekly sessions.[28]
De Sousa *et al.* in 2022 evaluated, by a randomized and controlled double-blind clinical trial on 18 patients with TMJD, the effects of PBM with the simultaneous use of red and infrared LED on pain and mandibular range of motion.
They concluded that LED wavelength association, even if it did not alter the mandibular range of motion, reduced pain.[29]
In 2023, Al-Quisi *et al.* compared red LED and Laser in temporomandibular pain reduction, concluding that red LED light and LASER therapies may effectively relieve symptoms associated with TMJD with no significant differences between their outcomes.[30]

### *Oral medicine*

While there are a significant number of studies about the utilization of laser PBM in Oral Medicine,[31,32] few are those regarding LED light.
De Carvalho *et al.* 2015 clinically and histologically evaluated the influence of Laser (660 nm) and LED (630 nm) PBM in the healing of formocresol-induced oral mucosa ulcers in rats.
They used 60 Wistar rats in which oral ulcers were induced on the gingiva of the lower incisors. They concluded that Laser and LED PBM effectively accelerated the healing of ulcers in both clinical and histological aspects.[33]
In 2014, Frere *et al.* performed an experimental study in Hamsters to compare the prevention and treatment of oral mucositis induced by chemotherapy.
The best results were obtained from the preventive laser (680 nm) and LED (670 nm) PBM groups and both treatments effectively diminished the OM lesions.[34]
Andrade *et al.*, in 2022, compared the utilization of PBM

to PDT as a co-adjuvant treatment of oral mucositis in oncologic subjects: they used blue LED (450 nm) and curcumin in a randomized trial study on 30 adult patients.
A reduction in the degree of mucositis and pain score was observed in the PBM and PDT groups, this last standing out when presenting early clinical improvement concerning the PBM group and the control group; regarding the antimicrobial effect, PDT showed a more significant reduction of yeasts of the genus Candida in the tested parameters.[35]

*Implantology*

Gokmenoglu *et al.*, in 2014, investigated the effect of LED PBM on implant osseointegration by measuring implant stability changes by resonance frequency analysis (RFA) and measuring interleukin-1 (IL-1 ), transforming growth factor- (TGF- ), prostaglandin-E2 (PGE2), and nitric oxide (NO) levels in peri-implant crevicular fluid (PICF). The study, conducted on fifteen patients irradiated by a wavelength of 626 nm, demonstrated that LED application to surgical areas positively affects the osseointegration process, so maintaining implant stability.[36]
In 2021, Kashefimehr *et al.*, in a split-mouth randomized clinical trial on twelve patients undergone bimaxillary immediate implant surgery with particulate bone grafts between the socket wall and the implant, showed that LED light led to a clinically significant increase in the implant stability quotient value after three months.[37]
Dalapria *et al.*, in 2022, studied the effect of PBM by 850 nm LED with and without a bone graft in forty-eight Wistar rats subjected to molar extraction, demonstrating that LED combined with the biomaterial improved bone formation in the histological analysis and diminished bone degeneration, so promoting an increase in bone density and volume. They concluded that LED may be an essential therapy to combine with biomaterials for promoting bone formation, along with the other known benefits of this therapy, such as for controlling pain and inflammatory process.[38]
These results were confirmed by Foletti *et al.* in 2023 by an *in vivo* study on 48 implants inserted in 8 Yucatan minipigs.[39] Histologic observations on bone tissues demonstrated that LED-PBM may improve and accelerate dental implant osseointegration: 25% of dental implants analyzed within the test group were completely osseointegrated, *versus* 12.5% within the control group.

*Periodontics*

Serrage *et al.*, in 2021, aimed to establish the potential immunomodulatory effects of blue and near-infrared light irradiation on gingival fibroblasts (GFs) essential cells involved in the pathogenesis of periodontitis. Cultures (*Escherichia coli, Fusobacterium nucleatum, Porphyromonas gingivalis*) were incubated overnight and subsequently irradiated using a bespoke radiometrically calibrated LED array (400-830 nm, irradiance: 24 $mW/cm^2$ dose: 5.76 $J/cm^2$) and effects of PBM on mitochondrial activity were assessed 24 h post-irradiation. The authors concluded that LED light may represent a promising approach in the management of the hyper-inflammatory response characteristic of periodontitis.[40]
Lee et al., in 2023, investigated by an *in-vitro* study the bactericidal and photobiomodulation effects of 470, 525, 590, 630, and 850 nm LED irradiation on *Streptococcus gordonii, Aggregatibacter actinomycetemcomitans, Fusobacterium nucleatum, Porphyromonas gingivalis,* and *Tannerella forsythia*. Nitric oxide, a proinflammatory mediator, levels were measured to identify the anti-inflammatory effect of LED irradiation on lipopolysaccharide-stimulated (LPS) inflammation in RAW 264.7 macrophages.
They concluded that LED irradiation at 470 nm showed bactericidal effects, while LED irradiation at 525 and 630 nm showed preventive and therapeutic effects on LPS-induced RAW 264.7 inflammation, suggesting the application of LED irradiation as an adjuvant in periodontal therapy.[41]

***Photodynamic therapy***

PDT oral application may be helpful in decontamination (endodontics, periodontics, and periimplantitis treatment) and for pre-malignant lesions non-invasive therapy.

*Periodontics and periimplantitis treatment*

Mongardini *et al.*, in 2014, in an *in vivo* study on 30 treated chronic periodontitis subjects, investigated the microbiological and clinical adjunctive outcome of a red LED device associated with toluidine blue, compared to scaling and root planning in maintenance supportive periodontal therapy (SPT).
Higher reductions of relative proportions of red complex bacteria were observed in test sites, showing that adjunc-

tive photodynamic treatment by LED light may enhance short-term clinical and microbiological outcomes in periodontitis subjects in SPT.[42]

In the same year, Cho *et al.* evaluated the effect of PDT using erythrosine and a green LED source on biofilms attached to resorbable blasted media (RBM) and sandblasted, large-grit, acid-etched (SLA) titanium surfaces *in vitro*.

They concluded that due to a significantly lower quantity of CFU/mL found in the PDT groups on both titanium disk surfaces as well as increased bacterial death observed in confocal scanning laser microscopy images, PDT using erythrosine and a green LED is effective in reducing the viability of *A. actinomycetemcomitans* attached to surface-modified titanium *in vitro*.[43]

Park *et al.*, in 2019, designed a non-invasive PDT with the ointment, which leads a photosensitizer deliverable into the gingival sulcus. They assessed whether 650 nm LED penetrates the 3-mm soft tissue and effectively activates toluidine-blue (TB) through the thickness to remove *Porphyromonas gingivalis* and *Fusobacterium nucleatum* species.

The efficacy of PDT was evaluated in *in-vitro* and *in vivo* models, and it was seen that four weeks of TB -PDT treatment significantly attenuated periodontitis-induced alveolar bone loss and inflammatory cytokines production in rats, confirming that a 650 nm LED indeed penetrates the gingiva and activates TB sufficiently delivered to and retained within the gingival sulcus: thus, it effectively kills the bacteria that reside around the gingival sulcus.

They concluded that TB-red LED PDT has the potential as a safe adjunctive procedure for periodontitis treatment.[44]

*Endodontics*

Asnaashari *et al.*, in 2015, investigated the antibacterial effects of PDT using an LED lamp (630 nm) and a diode laser (810 nm) on *E. faecalis* biofilms in anterior extracted human teeth.

Their *in-vitro* study, performed on fifty-six single-rooted extracted teeth, established that PDT could effectively supplement root canal disinfection with LED lamps more effectively than diode laser 810 nm.[45]

The same Authors, in 2017, compared a randomized controlled trial on 20 human subjects, LED-PDT (635nm) and calcium hydroxide therapy for root canal disinfection against *Enterococcus faecalis*, and their results showed that PDT and calcium hydroxide therapy, as auxiliary methods adjunct to conventional root canal therapy, are both effective in root canal disinfection; moreover, PTD caused a more significant reduction in *E. Faecalis* number in the infected root canals.[46]

Ali Mozayeni *et al.*, in 2020, compared the efficacy of three photosensitizers (toluidine blue, methylene blue, and curcumin) in PDT using LED against *Enterococcus faecalis* in root canal disinfection. The *ex-vivo* study involved 54 single-rooted extracted teeth, and the results showed that in all treatment groups, the mean values of colony forming unit (CFU) decreased by 99% compared to the control group. The authors concluded that the adjunction of Toluidine blue-mediated PDT through a LED light to NaOCl irrigation increased its antibacterial efficacy against *E. faecalis* and could be an effective complementary method in root canal disinfection.[47]

Shahbazi *et al.*, in 2022, reported a series of three endodontic cases treated with Toluidine Blue irradiated with a 630 nm LED lamp and concluded that PDT using LED lighting can be used in conjunction with conventional root canal treatment to achieve great results.[48]

*Pre-malignant lesions treatment*

Sulewska *et al.*, in 2019, evaluated the efficacy of PDT in the treatment of reticular oral lichen planus (OLP) by an *in vivo* study on fifty patients aged 26-84, with 124 OLP lesions in total, treated by 5-aminolevulinic acid (ALA) activated by a 630 nm LED light.

The therapy comprised ten weekly illumination sessions, and the lesions' response was macroscopically measured in millimeters with a periodontal probe and clinically evaluated at each session: on completion of the therapy, 109 sites improved, including 46 in complete remission, and the mean reduction in size was 62.91%.[49]

Di Stasio *et al.*, in 2020, investigated PDT as a minimally invasive method for treating oral leukoplakia (OL) through the activation of Toluidine blue as a topical photosensitizer and subsequent exposure to 630 nm LED light.

Eleven patients were evaluated at baseline (t0), at the end of treatment cycles (t1), and one year from the end of treatment (t2), and all the treated sites were photographed at each visit.

Results showed that at t1, complete response was obtained in six lesions, partial response in seven lesions, while only two lesions showed no response, and at t2, a further improvement was observed in two patients. The analysis of the areas showed a significant reduction of the lesion size from t0 to t1, suggesting that Toluidine blue appears to be a promising photosensitizer in the photodynamic therapy of oral leukoplakia.[50]

## Conclusions

As stated before, most of the Authors agree today that, regarding the photochemical effects on the tissues, Lasers and LEDs have the same behaviors.[7,8]
Nevertheless, LED light utilization offers some advantages which may be decisive in the choice by the practitioner.
First of all, in the case of treating a large area of tissue, the absence of collimation, a characteristic of Laser, allows simultaneous irradiation of LED light all the surface, saving time for the operator.
Moreover, LED technology is elementary and consequently also the cost when compared to laser devices.
Third, from a safety point of view, LED is free of risk, particularly for eyes, and so it does not require particular rules, such as glass, which is instead observed with Laser.
The use of LED in dentistry is not yet too popular due to the few clinical trials as well as of dental devices for oral utilization.
Even if more studies will be necessary to confirm the results above and, also to reach a consensus regarding indications, parameters, and what sensitizer/wavelength associations to use.
This new approach in dentistry may represent a great help for treating a large number of diseases with low costs and without side effects.

**Contributions:** Carlo Fornaini: investigation, writing – review & editing; Jean-Paul Rocca: writing – original draft; Huichao Wang: validation, writing – review & editing; YuPu Li: supervision, writing – review & editing. All the authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

**Conflict of interest:** the authors have no conflict of interest to declare.

**Ethics approval and consent to participate:** not applicable.

**Availability of data and materials:** all data generated or analyzed during this study are included in this published article.

**Funding:** this study received no specific funding.

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