PACT® 400

Scientific studies

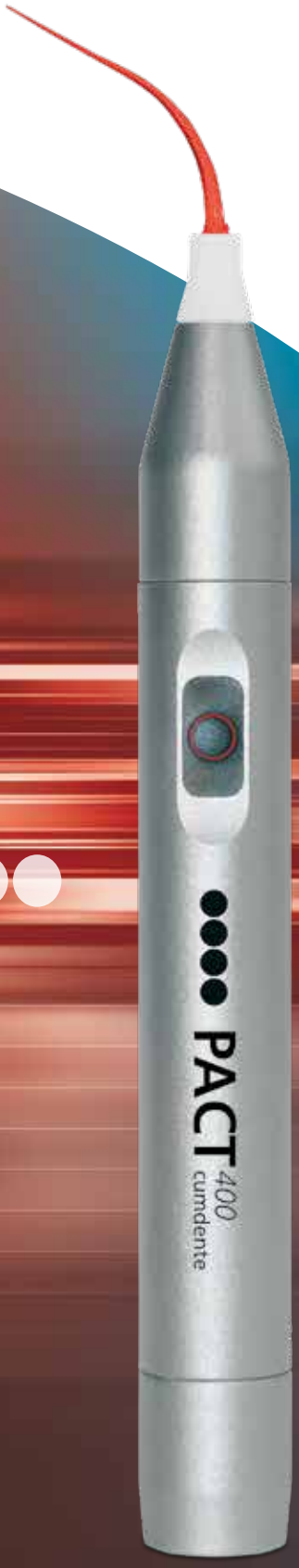

Photo Dynamic
Antimicrobial Therapy

www.cumdente.com

PACT

The following Abstracts of clinical studies are only a short list out of a high number of studies done in the field of photo-activated antimicrobial chemo therapy (PACT). We recommend to find more studies under http://www.ncbi.nlm.nih.gov/pubmed.

PACT Reviews

Smiley CJ, Tracy SL, Abt E, Michalowicz BS, John MT, Gunsolley J, Cobb CM, Rossmann J, Harrel SK, Forrest JL, Hujoel PP, Noraian KW, Greenwell H, Frantsve-Hawley J, Estrich C, Hanson N.
Systematic review and meta-analysis on the nonsurgical treatment of chronic periodontitis by means of scaling and root planing with or without adjuncts.
J Am Dent Assoc. 2015 Jul;146(7):508-24.
BACKGROUND: Conduct a systematic review and meta-analysis on nonsurgical treatment of patients with chronic periodontitis by means of scaling and root planing (SRP) with or without adjuncts. **METHODS:** A panel of experts convened by the American Dental Association Council on Scientific Affairs conducted a search of PubMed (MEDLINE) and Embase for randomized controlled trials of SRP with or without the use of adjuncts with clinical attachment level (CAL) outcomes in trials at least 6 months in duration and published in English through July 2014. The authors assessed individual study bias by using the Cochrane Risk of Bias Tool and conducted meta-analyses to obtain the summary effect estimates and their precision and to assess heterogeneity. The authors used funnel plots and Egger tests to assess publication bias when there were more than 10 studies. The authors used a modified version of the US Preventive Services Task Force methods to assess the overall level of certainty in the evidence. **RESULTS:** The panel included 72 articles on the effectiveness of SRP with or without the following: systemic antimicrobials, a systemic host modulator (subantimicrobial-dose doxycycline), locally delivered antimicrobials (chlorhexidine chips, doxycycline hyclate gel, and minocycline microspheres), and a variety of nonsurgical lasers (photodynamic therapy with a diode laser, a diode laser, neodymium:yttrium-aluminum-garnet lasers, and erbium lasers). **CONCLUSIONS AND PRACTICAL IMPLICATIONS:** With a moderate level of certainty, the panel found approximately a 0.5-millimeter average improvement in CAL with SRP. Combinations of SRP with assorted adjuncts resulted in a range of average CAL improvements between 0.2 and 0.6 mm over SRP alone. The panel judged the following 4 adjunctive therapies as beneficial with a moderate level of certainty: systemic subantimicrobial-dose doxycycline, systemic antimicrobials, chlorhexidine chips, and photodynamic therapy with a diode laser. There was a low level of certainty in the benefits of the other included adjunctive therapies. The panel provides clinical recommendations in the associated clinical practice guideline.

Azaripour A, Dittrich S, Van Noorden CJF, Willershausen B.
Efficacy of photodynamic therapy as adjunct treatment of chronic periodontitis: a systematic review and meta-analysis.
Feb;33(2):407-423.
Abstract: Meta-analysis of treatment effects of antimicrobial photodynamic therapy (aPDT) adjunct to non-surgical scaling and root planing (SRP) in comparison to SRP alone on patients with chronic periodontitis. The meta-analysis was performed according to PRISMA statement and Cochrane Collaboration guidelines. Electronic search complemented by hand search assured a high yield of randomized controlled trials (RCTs) of aPDT as adjunct modality to SRP. Differences in probing depth (PD) and clinical attachment level (CAL) were calculated with 95% confidence intervals and pooled in a random effects model. Analysis for intra- and inter-study heterogeneity was provided by $\chi 2$ and I 2 tests, and publication bias was checked by funnel plots. Pooled overall effects of 26 RCTs attested significant benefits of aPDT adjunct to SRP with respect to PD reduction (MD 0.37; 95% CI 0.12-0.53; $P < 0.0001$) and CAL gain (MD 0.33; 95% CI 0.19-0.48; $P < 0.00001$) after 3 and 6 months. Sensitivity analysis minimized heterogeneity of PD reduction (MD 0.21; 95% CI 0.13-0.30; $P < 0.00001$) and CAL gain (MD 0.36; 95% CI 0.27-0.46). aPDT adjunct to SRP provides significant PD reduction and CAL gain in treatment of chronic periodontitis. This moderate effect was found after 3 and 6 months which is short from a clinical perspective.

Chambrone L, Wang HL, Romanos GE.
Antimicrobial photodynamic therapy for the treatment of periodontitis and peri-implantitis: An American Academy of Periodontology best evidence review.
J Periodontol. 2018 Jul;89(7):783-803.
Abstract
BACKGROUND:
This systematic review evaluates the efficacy of antimicrobial photodynamic therapy (aPDT), as an adjunct to non-surgical or surgical therapy, on clinical and patient-centered outcomes in patients with periodontitis or peri-implantitis. **METHODS:** Randomized controlled trials (RCTs) with a follow-up duration ≥ 3 months that evaluated mechanical root/implant surface debridement (i.e., scaling and root planing [SRP] or implant surface scaling [ISS]) versus SRP or ISS plus aPDT for the treatment of adult patients (≥ 18 years old) with moderate-to-severe chronic (CP)/aggressive periodontitis (AgP) or peri-implantitis, respectively, were considered eligible for inclusion. The MEDLINE, EMBASE, and CENTRAL databases were searched for articles published up to and including March 2017. Random-effects meta-analyses were used throughout the review using continuous data (i.e., mean changes from baseline), and pooled estimates were expressed as weighted mean differences with their associated 95% confidence intervals. Additionally, summaries are presented of the included RCTs, critical remarks of the literature, and evidence quality rating/strength of recommendation of laser procedures. **RESULTS:** Of 729 potentially eligible articles, 28 papers (26 studies) were included in the review. Individual study outcomes and four sets of meta-analysis showed potential statistical significant benefit of aPDT in improving clinical attachment level (CAL) (non-surgical treatment of AgP) and probing depth (PD) (non-surgical treatment of AgP and CP). However, the comparative differences in clinical outcomes were modest (< 1 mm), and the level of certainty for different therapies was considered low-to-moderate (i.e., more information would be necessary to allow for a reliable and definitive estimation of effect/magnitude of therapies on health outcomes). Overall, most of the strengths of clinical recommendations of aPDT were guided by the expert opinion. **CONCLUSIONS:** aPDT may provide similar clinical improvements in PD and CAL when compared with conventional periodontal therapy for both periodontitis and peri-implantitis patients. The restricted base of evidence for some treatment approaches and conditions precludes additional conclusions.

PACT for the Treatment of Periodontitis and Periimplantitis

Cappuyns I, Cionca N, Wick P, Giannopoulou C, Mombelli A.
Treatment of residual pockets with photodynamic therapy, diode laser, or deep scaling. A randomized, split-mouth controlled clinical trial.
Lasers Med Sci. 2012 Sep;27(5):979-86. Epub 2011 Nov 22.
The objective of this work was to compare the effects of antimicrobial photodynamic therapy (PDT), diode soft laser therapy (DSL), and thorough deep scaling and root planing (SRP) for treatment of residual pockets. Thirty-two subjects with a history of non-surgical treatment for chronic periodontitis were included. Residual pockets >4 mm and bleeding upon probing were debrided with an ultrasonic device and then subjected to either PDT, DSL, or SRP. Pocket probing depth (PPD), bleeding on probing (BOP), and gingival recession were monitored over 6 months. Counts of four microorganisms were determined by direct hybridization with RNA probes. PPD decreased from 5.6 ± 1.0 to 3.8 ± 1.1 in 6 months ($p < 0.001$), and BOP decreased from 100% to 52% ($p < 0.01$). The risk for a site to remain >4 mm with BOP depended on initial PPD ($p = 0.036$) and was higher if treated with DSL ($p = 0.034$). Frequencies of three microorganisms were significantly lower in PDT- and SRP-treated than in DSL-treated quadrants ($p = 0.02$) after 14 days, but not at months 2 and 6. All three treatments resulted in a significant clinical improvement. PDT and SRP suppressed Porphyromonas gingivalis, Tannerella forsythia, and Treponema denticola stronger, and resulted in fewer persisting pockets after 6 months, than DSL application.

Schär D, Ramseier CA, Eick S, Arweiler NB, Sculean A, Salvi GE.
Anti-infective therapy of peri-implantitis with adjunctive local drug delivery or photodynamic therapy: six-month outcomes of a prospective randomized clinical trial.
Clin Oral Implants Res. 2012 May 9. [Epub ahead of print]
OBJECTIVE: To compare the adjunctive clinical effects in the non-surgical treatment of peri-implantitis with either local drug delivery (LDD) or photodynamic therapy (PDT). **MATERIAL AND METHODS:** Forty subjects with initial peri-implantitis, i.e. pocket probing depths (PPD) 4-6 mm with concomitant bleeding on probing (BoP) and marginal bone loss ranging from 0.5 to 2 mm between delivery of the reconstruction and pre-screening appointment were randomly assigned to two treatment groups. All implants underwent mechanical debridement with titanium curettes, followed by a glycine-based powder airpolishing. Implants in the test group (n = 20) received adjunctive PDT, whereas minocycline microspheres were locally delivered into the peri-implant pockets of control implants (n = 20). At sites with residual BoP, treatment was repeated after 3 and 6 months. The primary outcome variable was the change in the number of sites with BoP. Secondary outcome variables were changes in PPD, in clinical attachment level (CAL), and in mucosal recession (REC). **RESULTS:** After 3 months, implants of both groups yielded a statistically significant reduction ($P < 0.0001$) in the number of BoP-positive sites compared with baseline (LDD: from 4.41 ± 1.47 to 2.20 ± 1.28, PDT: from 4.03 ± 1.66 to 2.26 ± 1.28). After 6 months, complete resolution of mucosal inflammation was obtained in 15% of the implants in the control group and in 30% of the implants in the test group ($P = 0.16$). After 3 months, changes in PPD, REC, and modified Plaque Index (mPII) were statistically significantly different from baseline ($P < 0.05$). No statistically significant changes ($P > 0.05$) occurred between 3 and 6 months. CAL measurements did not yield statistically significant changes ($P > 0.05$) in both groups during the 6-month observation time. Between-group comparisons revealed no statistically significant differences ($P > 0.05$) at baseline, 3 and 6 months with the exception of the mPII after 6 months. **CONCLUSIONS:** In cases of initial peri-implantitis, non-surgical mechanical debridement with adjunctive use of PDT is equally effective in the reduction of mucosal inflammation

as with the adjunctive use of minocycline microspheres up to 6 months. Adjunctive PDT may represent an alternative treatment modality in the non-surgical management of initial peri-implantitis. Complete resolution of inflammation, however, was not routinely achieved with either of the adjunctive therapies.

Rühling A, Fanghänel J, Houshmand M, Kuhr A, Meisel P, Schwahn C, Kocher T.
Photodynamic therapy of persistent pockets in maintenance patients-a clinical study.
Clin Oral Investig. 2010 Dec;14(6):637-44**.**
The aim of this study was to compare the short-term performance of a session of single photodynamic therapy (PDT) and of a conventional ultrasonic debridement (UST) in persistent pockets of maintenance patients. In a prospective, randomized, controlled, single-blind clinical study, patients with chronic periodontitis with at least two persistent pockets (>4 mm) were enrolled. They were treated either with UST (n = 29) or PDT (n = 25). Clinical and microbiological examinations were performed at baseline and after 3 months. For UST, the mean probing depth was reduced from 5.3 to 4.5 mm (p =<0.001) and for PDT from 5.3 to 4.7 mm (p<0.001) with no difference between the two treatment modalities. Microbial counts were significantly reduced about 30% to 40% immediately after debridement but returned to baseline values a 3 months irrespective of treatment. PDT is not superior to conventional mechanical treatment of persistent pockets, but it may be a meaningful therapeutic alternative; the clinical effects were too minor to draw a definitive conclusion.

Andersen R, Loebel N, Hammond D, Wilson M.
Treatment of periodontal disease by photodisinfection compared to scaling and root planing.
J Clin Dent. 2007;18(2):34-8.
OBJECTIVE: The aim of the present study was to compare the effectiveness of a photodisinfection process to that of scaling and root planing (SRP) for non-surgical periodontal treatment. **METHODOLOGY:** Thirty-three subjects with moderate to advanced periodontal disease were randomly treated in one of three study arms with either photodisinfection (PD) alone (Group 1) using a diode laser and photosensitizer combination, with SRP alone (Group 2), or with SRP and PD combined (Group 3). Clinical assessments of bleeding on probing (BOP), probing pocket depth (PPD), and clinical attachment level (CAL) were made at baseline, three weeks, six weeks, and 12 weeks following therapy. **RESULTS:** No difference in any of the investigated parameters was observed at baseline between the three groups. The mean value of BOP decreased in the PD group (Group 1) from baseline by 71% at six weeks and 73% at 12 weeks, and in the SRP alone group (Group 2) from baseline by 43% at six weeks and 56% at 12 weeks. The BOP in the combined SRP + PD group (Group 3) decreased from baseline by 65% at six and 59% at 12 weeks. The sites treated with PD alone demonstrated mean CAL gains of 0.09 +/- 0.38 mm and 0.14 +/- 0.65 mm at six and 12 weeks, respectively. Those sites treated with SRP alone demonstrated mean CAL gains of 0.37 +/- 0.34 mm and of 0.36 +/- 0.35 mm at six and 12 weeks, respectively. The final group of SRP + PD demonstrated mean CAL gains of 0.92 +/- 0.62 mm and 0.86 +/- 0.61 mm at six and 12 weeks, respectively (p < 0.01 for six weeks and p < 0.02 for 12 weeks when compared to SRP alone). The sites treated with PD alone demonstrated mean PPD reductions of 0.69 +/- 0.33 mm and of 0.67 +/- 0.44 mm at six and 12 weeks, respectively. Those sites treated with SRP alone demonstrated mean PPD reductions of 0.78 +/- 0.47 mm and 0.74 +/- 0.43 mm at six and 12 weeks, respectively. The final group of SRP + PD demonstrated mean PPD reductions of 1.16 +/- 0.39 mm and 1.11 +/- 0.53 at six and 12 weeks, respectively (p < 0.06 for six weeks and p < 0.05 for 12 weeks when compared to SRP alone). **CONCLUSION:** Within the limits of the present study, it can be concluded that SRP combined with photodisinfection leads to significant improvements of the investigated parameters over the use of SRP alone.

Luan XL, Qin YL, Bi LJ, Hu CY, Zhang ZG, Lin J, Zhou CN.
Histological evaluation of the safety of toluidine blue-mediated photosensitization to periodontal tissues in mice.
Lasers Med Sci. 2008 Feb 1. [Epub ahead of print]
Our previous in vitro study has shown that toluidine blue (TB)-mediated lethal photosensitization of periodontal pathogens (PPs) from periodontal patients is possible. The purpose of this study was to investigate whether TB-mediated photosensitization exerted damaging effects on periodontal tissues in mice. Twenty-four mice were randomly divided into four groups; the experimental photodynamic therapy (PDT) group was treated with 1 mg/ml TB and light irradiation (60 J/cm(2), 635 nm, 337 s). Those in control groups were subjected to 140 J/cm(2) laser irradiation alone or to 2.5 mg/ml TB alone or received neither TB nor light exposure. All the mice were killed 72 h after they had been subjected to PDT, and periodontal tissue samples were taken for histological examination. During the 72 h observation period, no mice showed any distress. No necrotic or inflammatory changes were found in the gingiva, dentin, dental pulp or alveolar bone of the mice in any of the groups in this study. The results suggest that TB-mediated PDT is a safe antimicrobial approach for the treatment of periodontopathy without damaging effects to adjacent normal tissues.

Braun A, Dehn C, Krause F, Jepsen S.
Short-term clinical effects of adjunctive antimicrobial photodynamic therapy in periodontal treatment: a randomized clinical trial.
J Clin Periodontol. 2008 Oct;35(10):877-84
OBJECTIVE: The aim of this study was to assess the effect of adjunctive antimicrobial photodynamic therapy (aPDT) in chronic periodontitis. **MATERIAL AND METHODS:** Twenty patients with untreated chronic periodontitis were included. All teeth received periodontal treatment comprising scaling and root planing. Using a split-mouth design, two quadrants (test group) were additionally treated with aPDT. Sulcus fluid flow rate (SFFR) and bleeding on probing (BOP) were assessed at baseline, 1 week and 3 months after treatment. Relative attachment level (RAL), probing depths (PDs) and gingival recession (GR) were evaluated at baseline and 3 months after treatment. **RESULTS:** Baseline median values for PD, GR and RAL were not different in the test group and control group. Values for RAL, PD, SFFR and BOP decreased significantly 3 months after treatment in the control group (median delta RAL: -0.35 mm, inter-quartile range: 0.21 mm), with a higher impact on the sites treated with adjunctive aPDT (median delta RAL: -0.67 mm, inter-quartile range: 0.36 mm, p<0.05). GR increased 3 months after treatment with and without adjunctive aPDT (p<0.05), with no difference between the groups (p>0.05). **CONCLUSIONS:** In patients with chronic periodontitis, clinical outcomes of conventional subgingival debridement can be improved by adjunctive aPDT.

de Oliveira RR, Schwartz-Filho HO, Novaes AB Jr, Taba M Jr.
Antimicrobial photodynamic therapy in the non-surgical treatment of aggressive periodontitis: a preliminary randomized controlled clinical study.
J Periodontol. 2007 Jun;78(6):965-73
BACKGROUND: The treatment of aggressive periodontitis has always presented a challenge for clinicians, but there are no established protocols and guidelines for the efficient control of the disease. **METHODS:** Ten patients with a clinical diagnosis of aggressive periodontitis were treated in a split-mouth design study to either photodynamic therapy (PDT) using a laser source with a wavelength of 690 nm associated with a phenothiazine photosensitizer or scaling and root planing (SRP) with hand instruments. Clinical assessment of plaque index (PI), gingival index (GI), bleeding on probing (BOP), probing depth (PD), gingival recession (GR), and relative clinical attachment level (RCAL) were made at baseline and 3 months after treatment with an automated periodontal probe. **RESULTS:** Initially, the PI was 1.0 +/- 0.5 in both groups. At the 3-month evaluation, the plaque scores were reduced and remained low throughout the study. A significant reduction of GI and BOP occurred in both groups after 3 months (P <0.05). The mean PD decreased in the PDT group from 4.92 +/- 1.61 mm at baseline to 3.49 +/- 0.98 mm after 3 months (P <0.05) and in SRP group from 4.92 +/- 1.14 mm at baseline to 3.98 +/- 1.76 mm after 3 months (P <0.05). The mean RCAL decreased in the PDT group from 9.93 +/- 2.10 mm at baseline to 8.74 +/- 2.12 mm after 3 months (P <0.05), and in the SRP group, from 10.53 +/- 2.30 mm at baseline to 9.01 +/- 3.05 mm after 3 months. **CONCLUSION:** PDT and SRP showed similar clinical results in the non-surgical treatment of aggressive periodontitis.

Lulic M, Leiggener Görög I, Salvi GE, Ramseier CA, Mattheos N, Lang NP.
One-year outcomes of repeated adjunctive photodynamic therapy during periodontal maintenance: a proof-of-principle randomized-controlled clinical trial. J Clin Periodontol.
2009 Aug;36(8):661-6. Epub 2009 Jun 25.
BACKGROUND: Single photodynamic therapy (PDT) has been effective in initial periodontal therapy, but only improved bleeding on probing (BoP) in maintenance patients after a single use. Repeated PDT has not been addressed. **OBJECTIVES:** To study the possible added benefits of repeated adjunctive PDT to conventional treatment of residual pockets in patients enrolled in periodontal maintenance. **MATERIAL AND METHODS:** Ten maintenance patients with 70 residual pockets [probing pocket depth (PPD)>or=5 mm] were randomly assigned for treatment five times in 2 weeks (Days 0, 1, 2, 7, 14) with PDT (test) or non-activated laser (control) following debridement. The primary outcome variable was PPD, and the secondary variables were clinical attachment level (CAL) and BoP. These were assessed at 3, 6 and 12 months following the interventions. **RESULTS:** Greater PPD reductions were observed in the test (-0.67 +/- 0.34; p=0.01) compared with the control patients (-0.04 +/- 0.33; NS) after 6 months. Significant CAL gain (+0.52 +/- 0.31; p=0.01) was noted for the test, but not in the control (-0.27 +/- 0.52; NS) patients after 6 months. BoP percentages decreased significantly in test (97-64%, 67%, 77%), but not control patients after 3, 6 and 12 months. **CONCLUSIONS:** Repeated (five times) PDT adjunctive to debridement yielded improved clinical outcomes in residual pockets in maintenance patients. The effects were best documented after 6 months.

PACT for Caries Sterilisation

de Freitas MTM, Soares TT, Aragão MGB, Lima RA, Duarte S, Zanin ICJ.
Effect of Photodynamic Antimicrobial Chemotherapy on Mono- and Multi-Species Cariogenic Biofilms: A Literature Review.
Photomed Laser Surg. 2017 May;35(5):239-245.
OBJECTIVE: The aim of this literature review is to study the effect of photodynamic antimicrobial chemotherapy (PACT) on mono- and multi-species cariogenic biofilms.
METHODS: To this purpose, the database, PubMed, was searched using the descriptors, photodynamic therapy, antimicrobial photodynamic chemotherapy, and photoinactivation, associated with the mandatory presence of the word biofilm. A total of 98 references published from 2003 to 2016 were selected. Moreover, literature reviews (15), investigations that did not have biofilms related to dental caries (65), and those that did not have Streptococcus mutans count as an outcome (7) were excluded, yielding a final amount of 11 publications. **RESULTS:** The results revealed that Toluidine Blue O was the most used photosensitizer. Among the sources of light, light-emitting diode was the choice, and the biofilm models varied between in vitro and in situ. Multi-species biofilms were more resistant to the antimicrobial effects of PACT due to the thickness and complexity they have, which impede the penetration of the photosensitizer. This fact may also be associated with the type of photosensitizer used as well as with the light exposure time since the antimicrobial effect seems to be dose dependent. Despite this, in all the included publications, the therapy was effective in reducing S. mutans count. **CONCLUSIONS:** This review demonstrated that under different conditions, PACT is effective in reducing S. mutans count in monospecies biofilms. Multi-species biofilms were more resistant to the antimicrobial action of the therapy, possibly due to their thickness and complexity.

Melo MA, Rolim JP, Passos VF, Lima RA, Zanin IC, Codes BM, Rocha SS, Rodrigues LK.
Photodynamic antimicrobial chemotherapy and ultraconservative caries removal linked for management of deep caries lesions.
Photodiagnosis Photodyn Ther. 2015 Dec;12(4):581-6
BACKGROUND: Ultraconservative removal of carious tissue is becoming increasingly highlighted for management of deep caries lesions, and combined with an antimicrobial photochemistry-based treatment modality (PACT), this approach can be enhanced favoring dental tissue repair and preservation. The aim was to investigate the effectiveness of PACT using a light emitting diode (LED) associated with a photosensitizer toluidine blue ortho (TBO) on deep caries lesions. **METHODS:** For that, a single blind, randomized, controlled, split-mouth clinical trial where 45 patients with at least two deep carious lesions on permanent posterior teeth was performed. The primary intervention was deep caries lesion management with disinfection of remaining dentin tissue using PACT. Bacterial counts were measured following treatments as the main outcome. The remaining dentinal samples of each lesion were treated with either non-PACT-control or PACT. The PACT procedure were characterized by 100 μg mL(-1) TBO followed by 94J cm(-2) LED irradiation. Samples of dentin were collected before and immediately after treatments for microbiological analysis of total viable bacteria, mutans streptococci and Lactobacillus spp. counts. Microbial reduction was data were submitted to unpaired t test (χ=5%). **RESULTS:** PACT led to statistically significant reductions in mutans streptococci (1.08 ± 1.20 log), Lactobacillus spp. (1.69 ± 1.37 log), and total viable bacteria (1.07 ± 1.01 log) compared to the control, which showed log reductions respectively of 0.05 ± 0.49, 0.52 ± 0.89, and 0.47 ± 0.77 for the same microorganisms. **CONCLUSION:** Dentin from deep carious lesions treated with PACT showed a decrease in cariogenic microbial load.

Rolim JP, de-Melo MA, Guedes SF, Albuquerque-Filho FB, de Souza JR, Nogueira NA, Zanin IC, Rodrigues LK.
The antimicrobial activity of photodynamic therapy against Streptococcus mutans using different photosensitizers.
J Photochem Photobiol B. 2012 Jan 5;106:40-6. Epub 2011 Oct 19.
Several photosensitizers have been used against oral bacteria without standardization. Singlet oxygen ((1)O(2)) is an aggressive chemical species that can kill cells through apoptosis or necrosis. Objective: to compare the antimicrobial activity of photodynamic therapy (PDT) with different photosensitizers at the same concentration against Streptococcus mutans. In addition, the (1)O(2) production of each photosensitizer was determined. The photosensitizers (163.5 μM) methylene blue (MB), toluidine blue ortho (TBO) and malachite green (MG) were activated with a light-emitting diode (LED; χ=636 nm), while eosin (EOS), erythrosine (ERI) and rose bengal (RB) were irradiated with a curing light (χ=570 nm). Light sources were operated at 24 J cm(-2). For each photosensitizer, 40 randomized assays (n=10 per condition) were performed under one of the following experimental conditions: no light irradiation or photosensitizer, irradiation only, photosensitizer only or irradiation in the presence of a photosensitizer. After treatment, serial dilutions of S. mutans were seeded onto brain heart infusion agar to determine viability in colony-forming units per milliliter (CFU mL(-1)). Generation of (1)O(2) was analyzed by tryptophan photooxidation, and the decay constant was estimated. Results were analyzed by one-way ANOVA and the Tukey-Kramer test ($p<0.05$). PDT with irradiation in the presence of the photosensitizers TBO and MG was effective in reducing S. mutans counts by 3 and 1.4 logs, respectively ($p<0.01$), compared to their respective untreated controls. MB generated 1.3 times more (1)O(2) than TBO, and both produced significantly higher concentrations of singlet oxygen than the other photosensitizers. Since in vitro bulk (1)O(2) production does not indicate that (1)O(2) was generated in the bacterial activity site, the bactericidal action against S. mutans cannot be related to in vitro singlet O(2) generation rate. In vitroS. mutans-experiments demonstrated TBO as the only photosensitizer that effectively reduced 99.9% of these microorganisms.

Lima JP, Sampaio de Melo MA, Borges FM, Teixeira AH, Steiner-Oliveira C, Nobre Dos Santos M, Rodrigues LK, Zanin IC.
Evaluation of the antimicrobial effect of photodynamic antimicrobial therapy in an in situ model of dentine caries.
Eur J Oral Sci. 2009 Oct;117(5):568-74.
Photodynamic antimicrobial therapy (PACT) promotes bacterial death as a result of the photosensitization of microbial components. This study evaluated the effect of PACT on dentine caries produced in situ. Over the course of 14 d, 20 volunteers wore intra-oral devices containing human dentine slabs that were treated 10 times daily with a 40% sucrose solution. Afterwards, the antimicrobial effect of toluidine blue O, associated with 47 or 94 J cm(-2) of a light-emitting diode, was evaluated. Before and after the treatments, dentine samples were analysed with regard to the total number of microorganisms, total streptococci, mutans streptococci, and lactobacilli. Significant reductions in the bacterial count were observed for PACT with both energy densities tested, with the following values observed for 47 and 94 J cm(-2) of irradiation: for total streptococci, 3.45 and 5.18; for mutans streptococci, 3.08 and 4.16; for lactobacilli, 3.24 and 4.66; and for total microorganisms, 4.29 and 5.43, respectively. The control, treated with 94 J cm(-2) of irradiation alone, was also effective against all bacteria. To conclude, PACT was effective in killing oral microorganisms present in dentine caries produced in situ and may be a useful technique for eliminating bacteria from dentine carious lesions before restoration.

Zanin IC, Gonçalves RB, Junior AB, Hope CK, Pratten J.
Susceptibility of Streptococcus mutans biofilms to photodynamic therapy: an in vitro study.
J Antimicrob Chemother. 2005 Aug;56(2):324-30
OBJECTIVES: The purpose of this study was to evaluate the antimicrobial effect of toluidine blue O (TBO), in combination with either a helium/ neon (HeNe) laser or a light-emitting diode (LED), on the viability and architecture of Streptococcus mutans biofilms. **METHODS:** Biofilms were grown on hydroxyapatite discs in a constant depth film fermentor fed with artificial saliva that was supplemented with 2% sucrose four times a day, thus producing a typical ‚Stephan pH curve'. Photodynamic therapy was subsequently carried out on biofilms of various ages with light from either the HeNe laser or LED using energy densities of between 49 and 294 J/cm(2). **RESULTS:** Significant decreases in the viability of S. mutans biofilms were only observed when biofilms were exposed to both TBO and light, when reductions in viability of up to 99.99% were observed with both light sources. Overall, the results showed that the bactericidal effect was light dose-dependent and that older biofilms were less susceptible to photodynamic therapy. Confocal laser scanning microscopy images suggested that lethal photosensitization occurred predominantly in the outermost layers of the biofilms. **CONCLUSIONS:** Photodynamic therapy may be a useful approach in the treatment of dental plaque-related diseases.

Burns T, Wilson M, Pearson G J
Effect of dentine and collagen on the lethal photosensitisation of Streptococcus mutans.
Caries Res. 1995; 29: 192-197
Conclusion: Effective killing of 10 7 cfu S mutans was achieved with a range of energy densities using both HeNe and GaAlAs lasers after passage of the light through demineralised dentine discs using two photosensitisers Toluidine Blue O and AlPcS. Similar kill levels were observed when S mutans was suspended in a collagen matrix prior to exposure to the photosensitiser and light. The results imply that lethal photosensitisation may be effective at killing S mutans in a carious lesion even when the organism is suspended in demineralised dentine.

Williams J A, Pearson G J, Colles M J, Wilson M
The effect of variable energy input from a novel light source on the photo-activated bactericidal of toluidine blue O on Streptococcus mutans.
Caries Res 2003; 37: 190-193
Summary: The study examined the effect of variable energy doses of light at 635nm from a novel delivery system using a 100mW diode laser and a photosensitiser. The system killed up to

Scientific studies

10 9cfu/ml S mutans in planktonic solution. The antibacterial action was directly proportional to the energy doses rather than power output. Energy dose of 1.8J killed 10% of bacteria present. Bacteria could be killed to significant levels within 30 seconds.

Williams J A, Pearson G J, Colles M J, Wilson M
The photo-activated antibacterial action of toluidine blue O in a collagen matrix and in carious dentine.
Caries Res 2004; 38: 530-536
Summary: Effective killing of S mutans imbedded in a collagen matrix was achieved using a photosensitiser TBO [10µg/ml] in conjunction with a 100mW 635nm diode laser with the light delivered via an isotropic tip. The results showed that Photo-Activated Disinfection can achieve appreciable kills of oral bacteria including S mutans when the organisms are embedded in a collagen gel or present in carious teeth.

Bonsor S J, Pearson G J
Current clinical applications of Photo-Activated Disinfection in restorative dentistry.
Dental Update 2006; 33(3): 143-153
Summary: Photo-Activated Disinfection has been successfully used in operative dentistry as a means of disinfecting residual softened caries where exposure is likely. This results in the removal of less tooth tissue and may improve the prognosis of treatment. In endodontics, PAD provides a means whereby canals can be effectively disinfected. This suggests that the dental surgeon can be confident that micro-organisms can be effectively killed prior to obturation and restoration. PAD has other potential applications and further ongoing research work is currently being conducted prior to its extrapolation to the clinical situation.

PACT for Root Canal Disinfection

Tennert C, Feldmann K, Haamann E, Al-Ahmad A, Follo M, Wrbas KT, Hellwig E, Altenburger MJ.
Effect of photodynamic therapy (PDT) on Enterococcus faecalis biofilm in experimental primary and secondary endodontic infections.
BMC Oral Health. 2014 Nov 4;14:132.
BACKGROUND: To determine the antibacterial effect of photodynamic Therapy on Enterococcus faecalis (E. faecalis) biofilms in experimentally infected human root canals in primary infections and endodontic retreatments. **METHODS:** One hundred and sixty single-rooted extracted teeth with one root canal were prepared using ProTaper instruments. Seventy specimens were left without root canal filling and autoclaved. The root canals of another 70 specimens were filled with Thermafil and AH Plus and the root canal fillings were removed after 24 hours using ProTaper D files and plasma sterilized. The specimens were infected with a clinical isolate of E. faecalis for 72 hours. Samples were taken using sterile paper points to determine the presence of E. faecalis in the root canals. The specimens were randomly divided into groups according to their treatment with 20 teeth each and a control. In the PDT group the teeth were treated using PDT, consisting of the photosensitizer toluidine blue and the PDT light source at 635 nm. In the NaOCl (sodium hypochlorite) group the root canals were rinsed with 10 mL of 3% NaOCl. In the NaOCl-PDT group the root canals were rinsed with 10 mL of 3% of sodium hypochlorite and then treated with PDT. Samples were taken after treatments using sterile paper points. Additionally, remaining root canal filling material was recovered from the root canal walls. Survival fractions of the samples were calculated by counting colony-forming units. A one-way analysis of variance (ANOVA) was applied to the data to assess the effect of different treatment techniques. **RESULTS:** Antimicrobial treatment of root canals caused a significant reduction of bacterial load in all groups. NaOCl irrigation eliminated E. faecalis most effectively. PDT alone was less effective compared to NaOCl irrigation and the combination of NaOCl irrigation and PDT. CFU levels recovered from the filling material after NaOCl irrigation of the root canals were 10fold higher compared to PDT and the combination of NaOCl irrigation and PDT.
CONCLUSIONS: Photodynamic therapy killed E. faecalis in experimental primary endodontic infections and retreated human root canals. PDT is an effective supplement in root canal disinfection, especially in endodontic retreatments.

Ng R, Singh F, Papamanou DA, Song X, Patel C, Holewa C, Patel N, Klepac-Ceraj V, Fontana CR, Kent R, Pagonis TC, Stashenko PP, Soukos NS.
Endodontic photodynamic therapy ex vivo.
J Endod. 2011 Feb;37(2):217-22.
INTRODUCTION: The objective of this study was to evaluate the antimicrobial effects of photodynamic therapy (PDT) on infected human teeth ex vivo.
METHODS: Fifty-two freshly extracted teeth with pulpal necrosis and associated periradicular radiolucencies were obtained from 34 subjects. Twenty-six teeth with 49 canals received chemomechanical debridement (CMD) with 6% NaOCl, and 26 teeth with 52 canals received CMD plus PDT. For PDT, root canal systems were incubated with methylene blue (MB) at concentration of 50 µg/mL for 5 minutes, followed by exposure to red light at 665 nm with an energy fluence of 30 J/cm(2). The contents of root canals were sampled by flushing the canals at baseline and after CMD alone or CMD+PDT and were serially diluted and cultured on blood agar. Survival fractions were calculated by counting colony-forming units (CFUs). Partial characterization of root canal species at baseline and after CMD alone or CMD+PDT was performed by using DNA probes to a panel of 39 endodontic species in the checkerboard assay.
RESULTS: The Mantel-Haenszel χ(2) test for treatment effects demonstrated the better performance of CMD+PDT over CMD (P = .026). CMD+PDT significantly reduced the frequency of positive canals relative to CMD alone (P = .0003). After CMD+PDT, 45 of 52 canals (86.5%) had no CFUs as compared with 24 of 49 canals (49%) treated with CMD (canal flush samples). The CFU reductions were similar when teeth or canals were treated as independent entities. Post-treatment detection levels for all species were markedly lower for canals treated by CMD+PDT than they were for those treated by CMD alone. Bacterial species within dentinal tubules were detected in 17 of 22 (77.3%) and 15 of 29 (51.7%) canals in the CMD and CMD+PDT groups, respectively (P = .034).
CONCLUSIONS: Data indicate that PDT significantly reduces residual bacteria within the root canal system, and that PDT, if further enhanced by technical improvements, holds substantial promise as an adjunct to CMD.

Silva LA, Novaes AB Jr, de Oliveira RR, Nelson-Filho P, Santamaria M Jr, Silva RA.
Antimicrobial photodynamic therapy for the treatment of teeth with apical periodontitis: a histopathological evaluation.
J Endod. 2012 Mar;38(3):360-6. Epub 2012 Jan 24.
INTRODUCTION: This study evaluated the in vivo response of apical and periapical tissues of dogs' teeth with apical periodontitis after one-session endodontic treatment with and without antimicrobial photodynamic therapy (aPDT).
METHODS: Sixty root canals with experimentally induced apical periodontitis were instrumented and assigned to 4 groups receiving aPDT and root canal filling (RCF) or not: group aPDT+/RCF+ (n = 20): aPDT (photosensitizer phenothiazine chloride at 10 mg/mL for 3 minutes and diode laser [χ= 660 nm, 60 mW/cm(2)] for 1 minute) and RCF in the same session; group aPDT+/RCF- (n = 10); group aPDT-/RCF+ (n = 20), and group aPDT-/RCF- (n = 10). Teeth were restored, and the animals were killed after 90 days. Sections from the maxillas and mandibles were stained with hematoxylin-eosin and Mallory trichrome and examined under light microscopy. Descriptive (ie, newly formed apical mineralized tissue, periapical inflammatory infiltrate, apical periodontal ligament thickness, and mineralized tissue resorption) and quantitative (ie, periapical lesion size and number of inflammatory cells) microscopic analysis was performed. Quantitative data were analyzed by the Kruskal-Wallis and Dunn tests (χ= .05).
RESULTS: In the aPDT-treated groups, the periapical region was moderately/severely enlarged with no inflammatory cells, moderate neoangiogenesis and fibrogenesis, and the smallest periapical lesions.
CONCLUSIONS: Although apical closure by mineralized tissue deposition was not achieved, the absence of inflammatory cells, moderate neoangiogenesis, and fibrogenesis in the periapical region in the groups treated with aPDT indicate that this can be a promising adjunct therapy to cleaning and shaping procedures in teeth with apical periodontitis undergoing one-session endodontic treatment.

Garcez AS, Nuñez SC, Hamblin MR, Ribeiro MS.
Antimicrobial effects of photodynamic therapy on patients with necrotic pulps and periapical lesion.
J Endod. 2008 Feb;34(2):138-42. Epub 2007 Dec 21
This study analyzed the antimicrobial effect of photodynamic therapy (PDT) in association with endodontic treatment. Twenty patients were selected. Microbiological samples were taken after accessing the canal, endodontic therapy, and PDT. At the end of the first session, the root canal was filled with Ca(OH)(2), and after 1 week, a second session of the therapies was performed. Endodontic therapy gave a mean reduction of 1.08 log. The combination with PDT significantly enhanced the reduction (1.83 log, p = 0.00002). The second endodontic session gave a similar diminution to the first (1.14 log), and the second PDT was significantly more effective than the first (p = 0.002). The second total reduction was significantly higher than the second endodontic therapy (p = 0.0000005). The total first + second reduction (3.19 log) was significantly different from the first combination (p = 0.00006). Results suggest that the use of PDT added to endodontic treatment leads to an enhanced decrease of bacterial load and may be an appropriate approach for the treatment of oral infections.

Fonseca MB, Júnior PO, Pallota RC, Filho HF, Denardin OV, Rapoport A, Dedivitis RA, Veronezi JF, Genovese WJ, Ricardo AL.

Photodynamic therapy for root canals infected with Enterococcus faecalis. Photomed Laser Surg. 2008 Jun;26(3):209-13.
OBJECTIVE: The aim of this study was to investigate the effects of photodynamic therapy (PDT) on endodontic pathogens by evaluating the decrease in numbers of Enterococcus faecalis colonies in the canals of extracted human teeth. **BACKGROUND DATA:** Failure in endodontics is usually related to inadequate cleaning and disinfection of the root canal system. This is due to the establishment of microorganisms in areas where the instruments and chemical agents used during root canal preparation cannot eliminate them. PDT is a complementary therapeutic method that could be used to eliminate these remaining bacteria. PDT is a process in which radiation acts on a dye that is applied to the target organism, resulting in bacterial death. **MATERIALS AND METHODS:** Forty-six uniradicular teeth had their canals contaminated with bacteria and were incubated for 48 h at 35 degrees C. After that, the teeth were divided into a control group (CG) and a test group (TG). The 23 CG teeth did not undergo any intervention, whereas in the TG the teeth received a solution of 0.0125% toluidine blue for 5 min followed by irradiation using a 50-mW diode laser (Ga-Al-As) at a wavelength of 660 nm. Bacterial samples were taken before and after irradiation. In each of the samples, the number of colony-forming units (CFU) was counted. **RESULTS:** The mean decrease in CFU was 99.9% in the TG, whereas in the CG an increase of 2.6% was observed. **CONCLUSION:** PDT was effective as a bactericidal agent in Enterococcus faecalis-contaminated root canals.

PACT for Soft Tissue Treatment

Casu C, Mannu C.
Atypical Afta Major Healing after Photodynamic Therapy.
Case Rep Dent. 2017;2017:8517470.
The aim of this study is to report a case of atypical Afta Major healing in a patient with recurrent aphthous stomatitis (SAR) with a type of photodynamic therapy. A female patient with SAR affected for about 2 years reported a history of hypothyroidism treated with Levothyroxine. The oral cavity clinical examination showed several major symptomatic ulcers, previously treated with topical and systemic therapies without any benefit. The largest of them is present for more than 40 days, in spite of topical cortisone applications, with significant pain symptoms reported by the patient. It was decided to perform a session of photodynamic therapy with a device that emits a LED light used in combination with a photosensitive reagent (Toluidine blue). The dye was applied on the entire surface of the lesion beyond the margins and even encroaching on healthy tissue. The light diode was turned on with a wavelength of 630 nm with cycles from 30 seconds, 10 consecutive times above it. After a few days, a curious phenomenon happened: healing of Afta Major starting from the center, which was almost completely healed towards the borders of the lesion. No previous literature reports this type of healing. Photodynamic therapy could be a successful treatment for SAR.

Fischoff D, Spivakovsky S.
Photodynamic therapy for symptomatic oral lichen planus.
Evid Based Dent. 2018 Oct;19(3):90-91
Data sourcesMEDLINE/PubMed, Scopus and ISI Web of knowledge, from date of inception up to July 2017. Hand searching of the reference lists of the included studies was performed.Study selectionRandomised (RCT) and non-randomised (n-RCT) controlled trials and controlled and comparative studies were included in patients more than 18 years old diagnosed with symptomatic oral lichen planus, histopathologically confirmed, on the use of photodynamic therapy (PDT) compared with corticosteroids, published in English.Data extraction and synthesisTwo authors independently assessed for inclusion and performed quality assessment of the included studies following the CONSORT statement followed by the overall estimation of the risk of bias. Data extraction was also done independently by two authors. The primary outcome was the effect of PDT on pain and clinical improvement.ResultsFive studies were included: three RCTs and two n-RCTs having between eight and 30 participants. Two studies used diode laser and three used light emitting diode (LED) and the duration of the radiation ranged between 30 seconds to ten minutes. Each study used a unique corticosteroid agent. Three studies used methylene blue, one toluidine blue and one 5-aminolevulinic acid as photosensitiser agent. Follow-up was between one and three months. The authors presented the results as a narrative review.ConclusionsThe limited present evidence suggests that PDT is an effective treatment option for the management of OLP by reduction in pain, burning and decrease in the size of the lesions.

Pinto AP, Rosseti IB, Carvalho ML, da Silva BGM, Alberto-Silva C, Costa MS.
Photodynamic Antimicrobial Chemotherapy (PACT), using Toluidine blue O inhibits the viability of biofilm produced by Candida albicans at different stages of development.
BACKGROUND: Candida albicans is an opportunistic fungus producing both superficial and systemic infections, especially in immunocompromised individuals. It has been demonstrated that C. albicans ability to form biofilms is a crucial process for colonization and virulence. Furthermore, a correlation between the development of drug resistance and biofilm maturation at Candida biofilms has been shown. Photodynamic Antimicrobial Chemotherapy (PACT) is a potential antimicrobial therapy that combines visible light and a non-toxic dye, known as a photosensitizer, producing reactive oxygen species (ROS) that can kill the treated cells. The objective of this study was to investigate the effects of PACT, using Toluidine Blue O (TBO) on the viability of biofilms produced by C. albicans at different stages of development.
METHODS: In this study, the effects of PACT on both biofilm formation and viability of the biofilm produced by C. albicans were studied. Biofilm formation and viability were determined by a metabolic assay based on the reduction of XTT assay. In addition, the morphology of the biofilm was observed using light microscopy. **RESULTS:** PACT inhibited both biofilm formation and viability of the biofilm produced by C. albicans. Furthermore, PACT was able to decrease the number of both cells and filamentous form present in the biofilm structure. This inhibitory effect was observed in both early and mature biofilms.
CONCLUSIONS: The results obtained in this study demonstrated the potential of PACT (using TBO) as an effective antifungal therapy, including against infections associated with biofilms at different stages of development.

Souza RC, Junqueira JC, Rossoni RD, Pereira CA, Munin E, Jorge AO.
Comparison of the photodynamic fungicidal efficacy of methylene blue, toluidine blue, malachite green and low-power laser irradiation alone against Candida albicans.
Lasers Med Sci. 2009 Jul 5. [Epub ahead of print]
This study was to evaluate specific effects of photodynamic therapy (energy density 15.8 J/cm(2), 26.3 J/cm(2) and 39.5 J/cm(2)) using methylene blue, toluidine blue and malachite green as photosensitizers and low-power laser irradiation on the viability of Candida albicans. Suspensions of C. albicans containing 10(6) cells/ml were standardized in a spectrophotometer. For each dye, 120 assays, divided into four groups according to the following experimental conditions, were carried out: laser irradiation in the presence of the photosensitizer; laser irradiation only; treatment with the photosensitizer only; no exposure to laser light or photosensitizer. Next, serial dilutions were prepared and seeded onto Sabouraud dextrose agar for the determination of the number of colony-forming units per milliliter (CFU/ml). The results were subjected to analysis of variance and the Tukey test ($P < 0.05$). Photodynamic therapy using the photosensitizers tested was effective in reducing the number of C. albicans. The number of CFU/ml was reduced by between 0.54 log(10) and 3.07 log(10) and depended on the laser energy density used. Toluidine blue, methylene blue and malachite green were effective photosensitizers in antimicrobial photodynamic therapy against C. albicans, as was low-power laser irradiation alone.

Marotti J, Aranha AC, Eduardo Cde P, Ribeiro MS.
Photodynamic therapy can be effective as a treatment for herpes simplex labialis.
Photomed Laser Surg. 2009 Apr;27(2):357-63.
BACKGROUND DATA AND OBJECTIVE: Herpes is a common infectious disease that is caused by human herpesviruses. Several treatments have been proposed, but none of them prevent reactivation of the virus. This article describes the use of photodynamic therapy (PDT) as a treatment for herpes lesions, and reports on four cases. **MATERIALS AND METHODS:** PDT was used as an adjuvant therapy for the treatment of herpes labialis in four patients. A special type of 0.01% (m/V) of methylene blue solution was applied to the vesicular stage of herpesviral disease and the lesions were irradiated with laser energy (wavelength 660 nm, energy density 120 J/cm(2), output power of 40 mW, 2 min per point, 4.8 J of energy/point, at four points). After 24 h the patients returned and phototherapy was repeated with the same equipment, this time with 3.8 J/cm(2) and 15 mW, for a total dose of 0.6 J. The same procedure was repeated 72 h and 1 wk later. **RESULTS:** Treatment with low-level laser therapy can be considered as an option in the treatment of herpes labialis, and decreases the frequency of vesicle recurrence and provides comfort for patients. No significant acute side effects were noted and the lesions healed rapidly. **CONCLUSION:** Treatment of herpes labialis with PDT was effective, had no side effects, and when associated with laser phototherapy, accelerated the healing process.

Cumdente

Deutschland / International
Cumdente GmbH
Paul-Ehrlich-Straße 11
72076 Tübingen, Germany
Fon +49 7071 97557 21
Fax +49 7071 97557 22
www.cumdente.com