Photodiagnosis and Photodynamic Therapy 26 (2019) 193–198

Contents lists available at ScienceDirect

Photodiagnosis and Photodynamic Therapy

journal homepage: www.elsevier.com/locate/pdpdt

In vitro comparison of the effect of photodynamic therapy with curcumin and methylene blue on *Candida albicans* colonies

Franak Daliri[a], Arash Azizi[a], Mehdi Goudarzi[b], Shirin Lawaf[c,*], Arash Rahimi[d]

[a] Oral Medicine Department, Faculty of Dentistry, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran
[b] Department of Microbiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[c] Prosthodontics Department, Faculty of Dentistry, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran
[d] Biophysics Department, Islamic Azad University, Science and Research Branch, Tehran, Iran

ARTICLE INFO

Keywords:
Photodynamic therapy
Curcumin
Methylene blue
Candida albicans
Lasers

ABSTRACT

Background and aim: *Candida albicans* (*C. albicans*) causes oral fungal infections. Considering the high prevalence of candidiasis, the toxicity of antifungal drugs, and the fungistatic property which develops drug-resistant species, the present study aimed to assess the effect of photodynamic therapy (PDT) with curcumin (CUR) and methylene blue (MB) photosensitizers and lasers with different exposure parameters on *C. albicans* colonies.
Materials and methods: In this in-vitro experimental study, 150 samples of *C. albicans* standard strain (ATCC 10231) were examined using different combinations of CUR and MB photosensitizers with and without 460-nm and 660-nm laser irradiation with different exposure parameters in 15 groups of 10 samples each. The samples were cultured in microplates containing Sabouraud Dextrose Agar (SDA) medium, and the colony-forming units (CFU) were counted after 24 h of incubation at 37 °C. Data were analyzed using one-way analysis of variance (ANOVA) and Tukey's test.
Results: The maximum number of colonies was noted in the positive control group (CFU = 201,500 ± 42,093), while the minimum number was detected in the 460-nm laser + 10.2% CUR group (CFU = 10,100 ± 2558), followed by the nystatin group (CFU = 22,300 ± 5578). There was a significant statistical difference between the 460-nm laser + CUR group and other studied groups ($P < 0.0001$).
Conclusion: The 460-nm laser in combination with CUR has the maximum antifungal efficiency against *C. albicans*.

1. Introduction

Candida albicans (*C. albicans*) causes opportunistic oral fungal infections and comprises approximately 80% of microorganisms isolated from oral lesions [1]. *C. albicans* is found in the normal flora of the gastrointestinal system and genitourinary tracts and causes a spectrum of superficial to systemic mucocutaneous infections whenever there is an imbalance between the host and this microorganism due to drugs, antibiotics, estrogen, prostheses, xerostomia, or poor oral hygiene [2,3].

The current and conventional treatment for oral fungal infections includes the recognition, diagnosis, and elimination of risk factors such as tobacco, long-term corticosteroids, poor oral and prosthesis hygiene, radiotherapy and chemotherapy (causing long-term xerostomia) as well as prescription of local and systemic antifungal drugs [1,4]. Nevertheless, in patients affected by human immunodeficiency virus (HIV), the treatment is extremely difficult and complicated due to frequent recurrences [5].

Several *Candida* species release proteinases, phospholipases, acidic metabolites, and toxic elements causing damage to the structure and function of cells. Also, antifungal drugs can be toxic to the host and can develop drug-resistant species due to the fungistatic property. They can also induce hepatotoxicity in the elderly. In patients with a suppressed immune system, this microorganism can penetrate into the underlying tissues and blood vessels, causing life-threatening systemic infections. The morbidity and mortality rate associated with systemic candidiasis is approximately 30%–50% [2,4–6].

Photodynamic therapy (PDT) is a novel therapeutic strategy based on the interaction between a nontoxic photosensitizer and a safe source of visible light at a low intensity; the combination of these two factors in the presence of oxygen leads to the development of reactive oxygen species (ROS) which are toxic and cause oxidative damage to

* Corresponding author.
E-mail addresses: far0714@yahoo.com (F. Daliri), drarashazizi@yahoo.com (A. Azizi), gudarzim@yahoo.com (M. Goudarzi), drshlawaf@yahoo.com (S. Lawaf), arash_dds@yahoo.com (A. Rahimi).

https://doi.org/10.1016/j.pdpdt.2019.03.017
Received 4 January 2019; Received in revised form 19 March 2019; Accepted 22 March 2019
Available online 23 March 2019

Fig. 1. Preparation of Sabouraud Dextrose Agar (SDA) culture medium in Erlenmeyer flasks.

microorganisms and tumor cells [1,2]. Cells treated with photosensitizers in PDT are susceptible to eradication by exposure to light. Photosensitizers lack cytotoxicity but are activated following laser irradiation at a proper wavelength, leading to the development of ROS [7,8].

Curcumin (CUR) is activated by blue light and has antitumor, anticancer, anti-inflammatory, and antioxidative pharmacological properties as well as antimicrobial activities [9,10]. Since blue lasers have been recently introduced into the market and have several implications in soft tissue surgeries and since the effect of PDT mediated with blue laser and CUR extract on *C. albicans* has not yet been evaluated, the present study aimed to assess the effect of CUR- and MB-mediated PDT in combination with different laser exposure parameters on *C. albicans* colonies.

2. Materials and methods

In this in-vitro experimental study, 150 samples of *C. albicans* standard strain (ATCC 10,231) were prepared in 15 groups of 10 samples each in suspension form and were cultured in Sabouraud Dextrose Agar (SDA) medium (Fig. 1). After ensuring the purity of the culture, a new suspension with 0.5 McFarland turbidity (containing 1.5×10^8 CFU. ml^{-1}) was prepared (Fig. 2).

The aqueous extract of CUR at 10.2% concentration (Adonis Gol Darou Co., Alborz, Iran) and MB (Merck KGaA, Darmstadt, Germany) at 0.01% and 0.02% concentrations were diluted using a physiologic serum (Figs. 3 and 4). Next, 0.1 ml of *C. albicans* suspension was placed inside the wells of a 96-well microplate using a sampler; based on the sample, the same amount of photosensitizer or sterile physiologic serum was added. All these stages were performed under a laminar flow hood to provide a dark and sterile environment.

A diode laser (HamerzRad Electronic Industries Co., Iran) was used at 460-nm and 660-nm wavelengths. The power of the 460-nm laser was 25 mW, while the 660-nm laser had powers of 10 and 100 mW. The laser unit was calibrated at the beginning of the experiment. The laser was irradiated at a distance of 1 cm from the surface of the suspension. The samples were again cultured in SDA medium 5 min after PDT and were incubated at 37 °C for 24 h. Afterward, the colonies of *C. albicans* (CFU ml^{-1}) were counted (Fig. 5).

The studied groups:

1 Positive control group: the culture medium containing *C. albicans* without the use of photosensitizers or lasers (conventional treatment).
2 Negative control group: a pure culture medium without *C. albicans*.
3 10.2% CUR (102 mg/cc) was added to the suspension without laser irradiation.
4 A 460-nm laser with a 25-mW power was irradiated for 30 s without photosensitizers (sterile physiologic serum was added instead of the volume occupied by the photosensitizer).

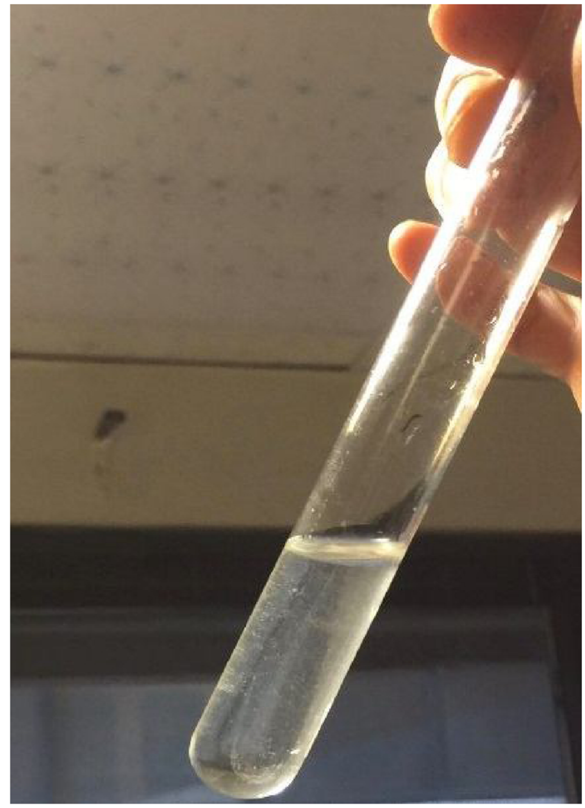

Fig. 2. *Candida albicans (C. albicans)* suspension with 0.5 McFarland turbidity.

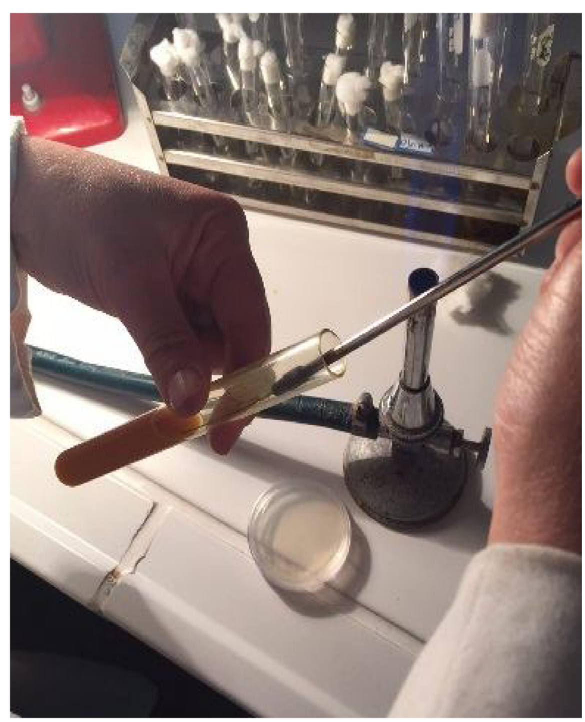

Fig. 3. Preparation of 10.2% aqueous extract of curcumin (CUR).

5 A 460-nm laser (25 mW) was irradiated for 30 s in combination with 10.2% CUR.
6 A 460-nm DC laser (25 mW) was irradiated for 60 s in combination with 10.2% CUR.

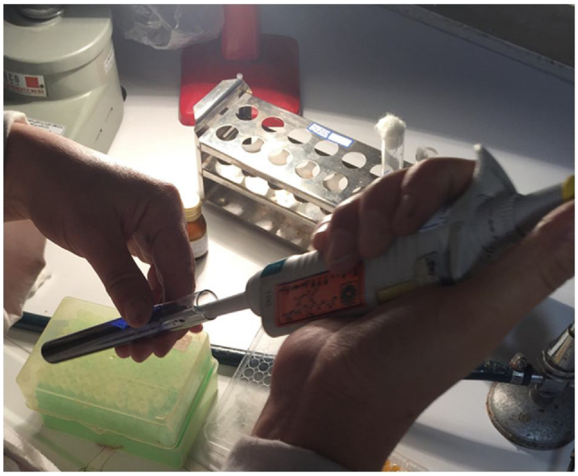

Fig. 4. Removal of methylene blue (MB) using a sampler for the preparation of 0.01% and 0.02% concentrations.

7 A 660-nm laser (100 mW) was irradiated for 100 s without photosensitizers (sterile physiologic serum was added instead of the photosensitizer).
8 A 660-nm laser (10 mW) was irradiated for 60 s without photosensitizers (sterile physiologic serum was added instead of the photosensitizer).
9 A 660-nm laser (100 mW) was irradiated for 100 s in combination with 0.02% MB.
10 A 660-nm laser (100 mW) was irradiated for 100 s in combination with 0.01% MB.
11 A 660-nm laser (10 mW) was irradiated for 60 s in combination with 0.01% MB.
12 0.02% MB without laser irradiation.
13 0.01% MB without laser irradiation.
14 Dental light-curing (Foshan Rixi Medical Equipment Industry Co. Ltd., China) at a 460-nm wavelength was performed for 120 s in combination with 10.2% CUR.
15 0.1 ml of nystatin (100,000 IU; Emad Darman Pars Co., Tehran, Iran) was added to 0.1 ml of *C. albicans* suspension.

After therapeutic interventions and PDT, the samples were cultured in SDA medium and were incubated at 37 °C for 24 h. The colonies (CFU ml^{-1}) were again counted [2].

Data were analyzed in SPSS 25 software (IBM Co., Chicago, IL, USA). Central dispersion indices of the number of *C. albicans* colonies related to different therapeutic protocols were determined. The differences in the number of colonies among different groups were analyzed using one-way analysis of variance (ANOVA), while Tukey's test was applied for pairwise comparisons (due to the distribution of the parameters). The rate of type I error was considered 0.05 in the present study.

3. Results

The central dispersion indices of *C. albicans* colonies are presented in Table 1. The experiment involved 15 groups including 13 experimental groups, one positive control group, and one negative control group (a total of 150 samples). The numbers of CFU according to the studied groups are presented in Table 1 which shows that:

-No colonies were detected in the negative control group (CFU = 0).

-CFU was equal to 201,500 ± 42,093 in the positive control group.

-The maximum number of colonies was associated with the positive control group (CFU = 201,500 ± 42,093) followed by CUR (CFU = 12,087 ± 92,900), while the minimum number of colonies was detected in the group irritated for 30 s by the 460-nm laser (25 mW) in combination with 10.2% CUR (CFU = 10,100 ± 2558); this difference was statistically significant ($P < 0.0001$).

ANOVA showed a statistically significant difference between the group of 460-nm/25-mW laser (30 s) + 10.2% CUR and other groups ($P < 0.0001$). Table 2 shows the results of pairwise comparisons of P-values in different therapeutic groups.

4. Discussion

The results of the present experimental study indicated that the maximum number of *C. albicans* colonies was detected in the positive control group (Mean CFU = 201,500 ± 42,093), while the minimum number of colonies was detected in the group of the continuous 460-nm laser + 10.2% CUR (mean CFU = 10,100 ± 2558). In other words, the highest therapeutic efficacy was achieved with diode laser irradiation at a 460-nm wavelength and a 25-mW power for 30 s in combination with CUR, which was significantly more efficient than the standard treatment with nystatin. Moreover, there were significant differences among different therapeutic groups in terms of the number of *C. albicans* colonies.

Pupo et al [11] used PDT as an alternative to antifungal drugs and achieved positive results. They assessed the effect of MB- and toluidine

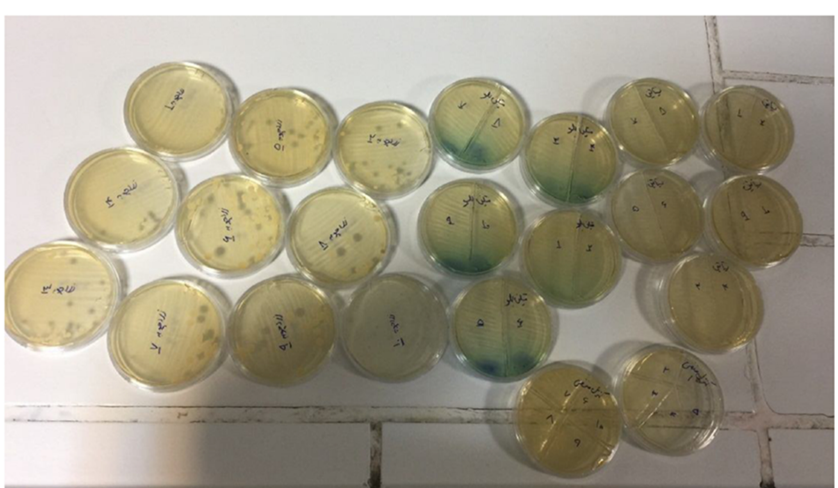

Fig. 5. Plates of different groups after 24 h of incubation.

Table 1
Central dispersion indices of *C. albicans* colony-forming units (CFU) in different groups.

Group	Mean	SD	Minimum	Maximum
460-nm laser + CUR	10100	2558.211	7000	14000
Nystatin	22300	5578.729	13000	30000
460-nm DC laser + CUR	27300	11576.317	10000	46000
460-nm laser	45200	19274.624	11000	67000
660-nm/100-mW laser (100 seconds) + 0.02% MB	55400	11682.846	35000	70000
660-nm/100-mW laser (100 seconds) + 0.01% MB	75300	20747.423	45000	106000
0.02% MB	75400	13133.503	54000	98000
0.01% MB	90800	19572.089	55000	118000
660-nm/10-mW laser (60 seconds) + 0.01% MB	74800	21988.886	41000	110000
660-nm/100-mW laser (100 seconds)	88000	15107.026	65000	110000
660-nm/10-mW laser (60 seconds)	69200	22826.885	43000	107000
LC + CUR	59200	30958.036	15000	100000
CUR	92900	12087.183	70000	110000
Negative control	0	0	0	0
Positive control	201500	42093.151	110000	260000

SD = Standard Deviation, CUR = Curcumin, MB = Methylene Blue, LC = Light-Curing.

blue (TB)-mediated PDT combined with diode laser (InGaAIP) irradiation (53 J/cm^2) on *C. albicans* colonies [11]. The results showed that the MB group and the laser group did not have significant differences with the positive control group, but the number of viable *C. albicans* cells significantly decreased after PDT, irrespective of the type of the photosensitizer [11]. Overall, their results are in line with ours, but in the present study, the type of the photosensitizer significantly affected the viability of *C. albicans*.

In a study by Dovigo et al [12] on 45 immunosuppressed rats in 5 groups, different concentrations of CUR (20, 40, and 80 μmol) were used, and the 80-μmol concentration in combination with a 455-nm light-emitting diode (LED) showed the maximum reduction in the number of *C. albicans* colonies. Also, the samples were histologically assessed, and it was concluded that CUR-mediated PDT can inactivate *C. albicans* without damaging hard tissues in rats [12].

Carmello et al [13] used a 455-nm laser in combination with CUR to produce singlet oxygen and destruct the DNA; they stated that PDT decelerated DNA repair more than did the separate use of blue light. The intracellular ROS synthesis was significantly higher in the group treated with blue light only. The comet tail, which is indicative of DNA destruction, was longer in the PDT group. In the group treated with light, the comet tail was reduced by 90% in the absence of light for 30 min, but in the PDT group, this reduction was equal to 45% [13]. The cited study was in line with ours in terms of the efficacy of PDT.

Fekrazad et al [14] evaluated the effect of phenothiazine dye (new MB) and indocyanine green (ICG; EmunDo®) combined with InGaAIP laser on *C. albicans* and concluded that PDT significantly decreases the viability of *C. albicans* compared to the control group, irrespective of the type of the photosensitizer and laser [14]. However, in our study, the type of the photosensitizer and laser affected the efficiency of PDT. Moreover, Fekrazad et al [14] reported that an increase in the output power and a decrease in the irradiation time of lasers are more suitable for the treatment goals.

Azizi et al [7] performed a study on 130 samples of *C. albicans* standard strain in 13 groups and reported that 808-nm laser irradiation at a pulse-repetition rate (PRR) of 100 Hz combined with ICG had the maximum efficiency in the reduction of *C. albicans* colonies with the mean CFU of 13,460 and log CFU of 4.12, which was slightly better than the results achieved with nystatin. However, in the present study, laser irradiation in combination with CUR showed significantly better results compared to other groups.

Table 2
The results of pairwise comparisons of P-values in different therapeutic groups.

Groups	Control-	Laser460 CW + CUR	Laser460 DC + CUR	Laser460	Laser660 + MB 0.02%	LC + CUR	Laser660, 10mW	Laser660, 10mW + MB 0.01%	Laser660, 100mW + MB 0.01%	MB 0.02%	Laser660,100mW	MB 0.01%	CUR	Nystatin	Control +
Control-	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Laser460 + CUR	0.0000	-	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Laser460 DC + CUR	0.0000	0.000	-	0.131	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	1.000	0.000
Laser460	0.0000	0.000	0.131	-	0.766	0.957	0.074	0.015	0.011	0.007	0.000	0.000	0.000	0.009	0.000
Laser660 + MB 0.02%	0.0000	0.000	0.000	0.766	-	1.000	0.991	0.871	0.821	0.732	0.132	0.092	0.047	0.000	0.000
LC + CUR	0.0000	0.000	0.001	0.957	1.000	-	0.897	0.587	0.514	0.410	0.038	0.024	0.011	0.000	0.000
Laser660,10mW	0.0000	0.000	0.000	0.074	0.991	0.897	-	1.000	1.000	1.000	0.882	0.813	0.656	0.000	0.000
Laser660, 10mW + MB 0.01%	0.0000	0.000	0.000	0.015	0.871	0.587	1.000	-	1.000	1.000	0.992	0.981	0.931	0.000	0.000
Laser660, 100mW + MB 0.01%	0.0000	0.000	0.000	0.011	0.821	0.514	1.000	1.000	-	1.000	0.997	0.990	0.957	0.000	0.000
MB 0.02%	0.0000	0.000	0.000	0.007	0.732	0.410	1.000	1.000	1.000	-	0.999	0.997	0.981	0.000	0.000
Laser660,100mW	0.0000	0.000	0.000	0.000	0.132	0.038	0.882	0.992	0.997	0.999	-	1.000	1.000	0.000	0.000
MB 0.01%	0.0000	0.000	0.000	0.000	0.092	0.024	0.813	0.981	0.990	0.997	1.000	-	1.000	0.000	0.000
CUR	0.0000	0.000	0.000	0.000	0.047	0.011	0.656	0.931	0.957	0.981	1.000	1.000	-	0.000	0.000
Nystatin	0.0000	0.000	1.000	0.009	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	-	0.000
Control +	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	-

CUR = Curcumin, MB = Methylene Blue, LC = Light-Curing.

Fabio et al [15] evaluated the impact of PDT with a 660-nm diode laser and 0.01% MB on 35 immunosuppressed rats in 7 groups and observed that the number of *C. albicans* colonies was equal in all groups on the third and fifth days, but on the seventh and eleventh days, the control group showed the highest number of colonies. The PDT group

The present study showed that the effects of CUR and blue laser were greater than the effects of MB and red laser in eliminating *C. albicans*. It should be noted that CUR has a greater penetrability in dental tissues and microorganisms, which makes its antimicrobial properties greater than that of other photosensitizers. Badaoui Strazzi Sahyon et al [20] showed that CUR changes the mechanical properties of intradentinal tubules during PDT.

exhibited the lowest number of colonies (log CFU = 3.23 ± 0.37); although this group showed better results than nystatin, the difference was not significant [15], which differs from our results

de Miranda and Colombo [16] demonstrated the positive effects of PDT in a randomized clinical trial (RCT). Mandibular molars of 32 patients with apical periodontitis were selected and evaluated in two groups of PDT and mechanical-chemical debridement. After taking 3- and 6-month follow-up radiographs, they reported a significantly diminished periapical repair in both groups, but the PDT group showed a better repair after 6 months compared to the control group [16].

Alves et al [17] assessed the antimicrobial effect of phenothiazine-mediated PDT in combination with a 660-nm LED (37.5 J/cm^2) on the virulence factors of fluconazole-susceptible and fluconazole-resistant *C. albicans* and reported that PDT decreased the viability of fluconazole-susceptible and fluconazole-resistant *C. albicans*. They also stated that the sensitivity of fluconazole-resistant *C. albicans* to PDT was lower, and PDT had no effect on adhesion, biofilm formation, and enzyme synthesis [17].

Hsieh et al [18] used CUR-mediated PDT and a 430-nm blue LED as an independent treatment and also in combination with fluconazole and concluded that fluconazole eliminated the yeast form of the fungus, while PDT eliminated the biofilm. As a result, the combination of fluconazole and CUR-mediated PDT can be used for preventing the growth and virulence of *C. albicans*; a more efficient result was observed in the fluconazole + PDT group [18].

As from the beginning of the 1980s, candidiasis has been a huge problem, especially in immunosuppressed patients, CUR was introduced as one of the alternative treatments [19].

In the study by Dovigo et al [12], CUR-mediated PDT eliminated *C. albicans* quite rapidly, while antifungal drugs need to be used for a few days to act.

Two mechanisms have been proposed for the phototoxicity of CUR including type I (formation of H2O2 and O2) and II (formation of singlet oxygen) [12].

The oxidative stress caused by ROS (superoxide, hydroxyl, and particularly singlet oxygen) damages the integrity of cells through damaging the DNA, lipids, proteins, and other cellular macromolecules and eventually causes cell death through necrosis or apoptosis [17–19]. Yeast cells are aerobic and synthesize ROS through natural metabolism in the mitochondrial respiratory chain and through peroxisomal metabolism, producing H2O2 during reactions catalyzed by oxidases.

The endogenous ROS disseminate from the mitochondrial electron transport chain, diffuse freely from the cell membrane, and attack other cellular components. The oxidative damage caused by the endogenous ROS induces an alkaline transition in the DNA, single/double-strand DNA breaks, and purine/pyrimidine damage, which may be toxic and mutagenic. The endogenous ROS and the ROS produced by light and CUR are responsible for the genetic damage of *C. albicans* cells [13].

In a recent study, CUR has been effective at concentrations lower than 1 mmol although its bioavailability is lost due to its poor solubility. The regenerative power of CUR can be improved by increasing its solubility through heat, diffusion, synthesis of nanoparticles, and metal chelation. Considering its efficiency, PDT has been used clinically on oral cancer and on other types of cancer although the difficulty of antifungal therapies is related to the eradication of fungal biofilms which play a role in virulence and drug resistance [18].

[20].

Another advantage of CUR-mediated PDT is its wide range of activity as it involves both type I and type II reactions; therefore, when the microorganism is still unidentified, CUR-mediated PDT can be used as the first-line treatment for a local infection [12].

In the present study, the standard strain of the microorganism has been used, which is different from the real situation.

In the nystatin group, culturing was performed after 5 min, similar to other groups; this time period may not have been enough for nystatin although, from the clinical aspect, patients use nystatin as a mouthwash and cannot keep it for long in the mouth.

The high number of groups and different treatment protocols are among the advantages of the present study.

This study was free of bias, and the person responsible for colony counting was blind to the study procedure.

According to the results of the present study, the lowest efficacy in the reduction of *C. albicans* colonies was recorded in the groups of CUR alone and MB alone. Accordingly, laser irradiation in PDT is necessary to decrease the number of *C. albicans*, and the separate use of photosensitizers is not efficient in these cases.

5. Conclusion

The results of the present study showed that a 460-nm/25-mW laser irradiated for 30 s in combination with CUR had the maximum antifungal efficiency against *C. albicans*.

Acknowledgements

Our appreciation is extended to the Dental Branch of Islamic Azad University, Tehran, Iran, and also to Mr. Naser Valaei, Dr. Mohammad Javad Kharazifard, and all who cooperated with us during the course of this study.

References

[1] F. Javed, L.P. Samaranayake, G.E. Romanos, Treatment of oral fungal infections using antimicrobial photodynamic therapy: a systematic review of currently available evidence, Photochem. Photobiol. Sci. 13 (May 5) (2014) 726–734.
[2] I.T. Kato, R.A. Prates, C.P. Sabino, B.B. Fuchs, G.P. Tegos, E. Mylonakis, et al., Antimicrobial photodynamic inactivation inhibits Candida albicans virulence factors and reduces in vivo pathogenicity, Antimicrob. Agents Chemother. 57 (January 1) (2013) 445–451.
[3] A.C. Costa, V.M. de Campos Rasteiro, C.A. Pereira, E.S. da Silva Hashimoto, M. Beltrame Jr, J.C. Junqueira, et al., Susceptibility of Candida albicans and Candida dubliniensis to erythrosine- and LED-mediated photodynamic therapy, Arch. Oral Biol. 56 (November 11) (2011) 1299–1305.
[4] H. Khademi, N. Torabinia, M. Allameh, H.R. Jebreilamtigh, Comparative evaluation of photodynamic therapy induced by two different photosensitizers in rat experimental candidiasis, Dent. Res. J. (Isfahan) 11 (July 4) (2014) 452–459.
[5] F. Freire, A.C. Costa, C.A. Pereira, M. Beltrame Junior, J.C. Junqueira, A.O. Jorge, Comparison of the effect of rose bengal- and eosin Y-mediated photodynamic inactivation on planktonic cells and biofilms of Candida albicans, Lasers Med. Sci. 29 (May 3) (2014) 949–955.
[6] R.C. Souza, J.C. Junqueira, R.D. Rossoni, C.A. Pereira, E. Munin, A.O. Jorge, 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. 25 (May 3) (2010) 385–389.
[7] A. Azizi, Z. Amirzadeh, M. Rezai, S. Lawaf, A. Rahimi, Effect of photodynamic therapy with two photosensitizers on Candida albicans, J. Photochem. Photobiol. B 158 (May) (2016) 267–273.
[8] A. Azizi, S. Shademan, M. Rezai, A. Rahimi, S. Lawaf, Effect of photodynamic therapy with two photosensitizers on Streptococcus mutants: in vitro study, Photodiagn. Photodyn. Ther. 16 (December) (2016) 66–71.
[9] S. Irshad, A. Muazzam, Z. Shahid, M.B. Dalrymple, Curcuma Longa (tumeric):an auspicious spice for antibacterial, photochemical and antioxidant activities, Pak. J. Pharma Sci. 31 (November 6 supplementary) (2018) 2689–2696 (رفرنس 9به مقاله اضافه شد.
[10] M.C. Andrade, A.P. Ribeiro, L.N. Dovigo, I.L. Brunetti, E.T. Giampaolo, V.S. Bagnato, et al., Effect of different pre-irradiation times on curcumin-mediated photodynamic therapy against planktonic cultures and biofilms of Candida spp, Arch. Oral Biol. 58 (February 2) (2013) 200–210.
[11] Y.M. Pupo, G.M. Gomes, E.B. Santos, L. Chaves, M.D. Michel, V.A. Kozlowski Jret al., Susceptibility of Candida albicans to photodynamic therapy using methylene blue and toluidine blue as photosensitizing dyes, Acta Odontol. Latinoam. 24 (2) (2011) 188–192.
[12] L.N. Dovigo, J.C. Carmello, C.A. de Souza Costa, C.E. Vergani, I.L. Brunetti, V.S. Bagnato, et al., Curcumin-mediated photodynamic inactivation of Candida albicans in a murine model of oral candidiasis, Med. Mycol. 51 (April 3) (2013) 243–251.
[13] J.C. Carmello, A.C. Pavarina, R. Oliveira, B. Johansson, Genotoxic effect of photodynamic therapy mediated by curcumin on Candida albicans, FEMS Yeast Res. 15 (June 4) (2015) fov018.
[14] R. Fekrazad, V. Ghasemi Barghi, Mir A. Poorsattar Bejeh, M. Shams-Ghahfarokhi, In vitro photodynamic inactivation of Candida albicans by phenothiazine dye (new methylene blue) and Indocyanine green (EmunDo®), Photodiagn. Photodyn. Ther. 12 (March 1) (2015) 52–57.
[15] C.A. Fabio, M.B. Yolanda, G.M. Carmen, C. Francisco, B. Antonio Julián, P.L. Leonor, et al., Use of photodynamic therapy and chitosan for inactivation of Candida albicans in a murine model, J. Oral Pathol. Med. 45 (September 8) (2016) 627–633.
[16] R.G. de Miranda, A.P.V. Colombo, Clinical and microbiological effectiveness of photodynamic therapy on primary endodontic infections: a 6-month randomized clinical trial, Clin. Oral Investig. 22 (May 4) (2018) 1751–1761.
[17] F. Alves, E.G. de Oliveira Mima, R.C.P. Passador, V.S. Bagnato, J.H. Jorge, A.C. Pavarina, Virulence factors of fluconazole-susceptible and fluconazole-resistant Candida albicans after antimicrobial photodynamic therapy, Lasers Med. Sci. 32 (May 4) (2017) 815–826.
[18] Y.H. Hsieh, J.H. Zhang, W.C. Chuang, Huang X.B. Yu KH, Y.C. Lee, et al., An in vitro study on the effect of combined treatment with photodynamic and chemical therapies on Candida albicans, Int. J. Mol. Sci. 24;19 (January 2) (2018) pii: E337.
[19] A. Azizi, S. Mousavian, S. Taheri, S. Lawaf, E. Gonoudi, A. Rahimi, Comparison of the antimicrobial efficacy of photodynamic therapy with two mediators against Lactobacillus acidophilus in vitro, Photodiagn. Photodyn. Ther. 21 (March) (2018) 357–362.
[20] Sahyon H. Badaoui Strazzi, P.P.D. Silva, M.S. de Oliveria, Cintra L. Tavares Angelo, E. Dezan Junior, J.E. Gomes-Filho, Influence of curcumin photosensitizer in photodynamic therapy on the mechanical properties and push- out bond strength of glass-fiber posts to intraradicular dentin, Photodiagn. Photodyn. Ther. 24 (January 18) (2019) 30335–30341, https://doi.org/10.1016/j.pdpdt.2019.01.025 [Epub ahead of print] pii: S1572-1000.