

RESEARCH PAPER

## Comparative efficacy of titanium dioxide nanoparticles loaded carboxymethyl cellulose and hydrogen peroxide gel on tooth whitening: An *in-vitro* study

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### ABSTRACT

**Objective(s):** In this study we evaluated the photocatalytic activity and dye degradation of blue light-activated and UV-activated carboxymethylcellulose gel containing titanium dioxide nanoparticles and compared with 40% hydrogen peroxide bleaching effect to reach to a new strategy that has most efficiency with minimal side effects.

**Materials and Methods:** The effective concentration of carboxymethylcellulose gel containing TiO<sub>2</sub> nanoparticles was determined. The color of the main samples was measured at first, after staining with coffee and after the bleaching process by colorimeter. E<sub>1</sub>, E<sub>2</sub>, E<sub>3</sub> were recorded and ΔE<sub>1</sub>, ΔE<sub>2</sub> were calculated. Samples were divided into eight groups, each containing six. In three groups, the bleaching effect of CMC gel containing TiO<sub>2</sub> nanoparticles irradiated with UV-C was investigated after one, two, and three times exposure to the teeth. In the other three groups, the bleaching effect of CMC gel containing TiO<sub>2</sub> nanoparticles irradiated with light cure was investigated after one, two, and three times exposure to the teeth. The results were compared with two control groups CMC and H<sub>2</sub>O<sub>2</sub>.

**Results:** The effective concentration of carboxymethylcellulose gel containing TiO<sub>2</sub> nanoparticles was 20%. ΔE<sub>2</sub> result for H<sub>2</sub>O<sub>2</sub> control group was 6.34 and for CMC control group was 2.54. The values of ΔE<sub>2</sub> in groups were exposed once, twice and three times to CMC gel containing TiO<sub>2</sub> nanoparticles that were activated by UV were 3.83, 4.19, 4.42 respectively and ΔE<sub>2</sub> results in groups were exposed once, twice and three times to CMC gel containing TiO<sub>2</sub> nanoparticles that were activated by blue-light were 4.45, 5.03, 5.55 respectively.

**Conclusion:** The greatest value of ΔE<sub>2</sub> belonged to the bleached group with hydrogen peroxide gel with ΔE<sub>2</sub>: 6.34 and after that related to the group activated three times with blue light with ΔE<sub>2</sub>: 5.55. All groups except the CMC control group showed ΔE<sub>2</sub> higher than 3.3.

**Keywords:** Blue light, Hydrogen peroxide, Titanium dioxide nanoparticles, Tooth bleaching, UV

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### INTRODUCTION

Patients are highly sensitive to aesthetics, including tooth color [1], leading to the introduction of several bleaching products and systems for the teeth [2]. Such products are among the most conservative dental treatments

[3]. Chromogens obtained from usually consumed foods (e.g., coffee, tea, chocolate, and tobacco) causes by extrinsic discoloration [4]. Over the years, several bleaching methods have been introduced to achieve subjectively whiter teeth [5], including in-office approaches and home-bleaching kits. Currently, the use of hydrogen peroxide prevails in dental practice [2]. Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) concentration and administration period have a major contribution to the success

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of in-office tooth whitening. However, the use of H<sub>2</sub>O<sub>2</sub> may cause some problems, including enamel demineralization, tooth sensitivity, gingival irritation, cytotoxicity, and acute pulpitis [6]. Various light sources are administered in combination with in-office bleaching products, to facilitate the rates of chemical reaction of the bleaching process [7]. According to the literature, light using halogen, light-emitting diode (LED), or laser can stimulate bleaching agents [8]. Such procedures result in the enhanced release of hydroxyl radicals through increased temperature [7]. Evidence regarding the effectiveness of light sources for in-office bleaching are inconsistent. In addition, its role in frequently administered bleaching procedures is not clear yet [9-14]. Apart from the contribution of light sources in enhancing the chemical reaction of bleaching gels, some studies investigated catalyzing molecules like titanium dioxide (TiO<sub>2</sub>), which is a major photocatalyst semiconductor in an extensive spectrum of environmental administrations. TiO<sub>2</sub> is an important photocatalyst agent because of its oxidizing characteristics, absence of toxicity, photo and chemical stability in a wide pH band [15], and commonly used as a whitening or brightening agent in various applications [16]. Nanoscale TiO<sub>2</sub> reinforcement agents bring new optical, electrical, physiochemical characteristics [17-19]. The administration of nanoparticles is on the rise in dentistry because of their antimicrobial and mechanical characteristics. In addition, because of their antibacterial characteristics, chemically inert, low price, high resistance, and hardness, TiO<sub>2</sub> nanoparticles are widely applied in manufacturing dental materials [20, 21]. The attention towards the administration of nanocrystalline TiO<sub>2</sub> as a photocatalyst for the degradation of organic pollutants has increased in recent decades [22]. Tooth exposure to light-curing units (LCUs) is one of the routine conditions in restorative dentistry [23]. Sensitivity results from the insult of the peroxide on the nerve may be considered reversible pulpitis [24]. Antimicrobial properties of TiO<sub>2</sub> nanoparticles and their application in Medicine, Dentistry, and other sciences have been widely known [25]. It is also safe for the human body [16, 26, 27]. Overall, gels containing nanoparticles are found to be less toxic compared to the products that are produced using hydrogen peroxide [2]. Carboxymethyl cellulose (CMC), is a biocompatible and biodegradable polymer, has been used in the biomedical field, also in paper, ceramic, and food industries [28, 29]. CMC as a traditional bio-absorbent, has a high chelating

characteristics, strong adsorption efficiency, and an acceptable capacity for cationic dyes. A synergistic effect of photocatalytic degradation by TiO<sub>2</sub> and electrostatic adsorption enrichment by CMC causes enhancement in photocatalytic activity [30].

In this study, the effect of TiO<sub>2</sub> nanoparticles on teeth (stained or discolored) using the photocatalytic power of these nanoparticles in whitening and removing colored deposits was used as a method for teeth whitening. For this purpose, titanium dioxide nanoparticles gel was used in CMC on the surface of stained teeth, and its whitening effect was compared with hydrogen peroxide. Teeth whitening was caused by the photocatalytic effect of titanium dioxide nanoparticles that was amplified by UV or blue light radiation.

## MATERIALS AND METHOD

### Materials

Chloramine T and TiO<sub>2</sub> Nanoparticles ( $\geq 99\%$  purity, size diameter  $\leq 100$ ) were purchased from Sigma-Aldrich and confirmed by Dynamic light scattering (DLS), Scanning Electron Microscope (SEM) and Energy Dispersive Spectroscopy (EDS) and shown in Fig. 1. Hydrogen peroxide gel (40%) obtained from (Opalescence Boost), Coffee (Gold), CMC purchased from (Kimia Tehran)

### Primary color measurement of samples

Six human premolars without cracks, surface defects, previous restorations, and anomalies that were extracted for orthodontic purposes were used in this study. A Minolta colorimeter (Konica Minolta model CR-400) and CIE L\*a\*b\* parameters analysis was used for measurement of tooth color. CIE L\*a\*b\* values were assessed using the reflectance evaluations, where L\* indicates lightness/darkness ( $\Delta L^*$ : the changes of lightness/darkness), a\* indicates redness/greenness ( $\Delta a^*$ : the changes of redness/greenness) and b\* indicates yellowness/blueness ( $\Delta b^*$ : the changes of yellowness/blueness). The area selected for color determination was the middle part of the buccal surface of the teeth.

### Preparing and coloring samples

The samples were kept in 0.05% chloramine T solution for one week. Then, for simulation, they were placed in coffee solution for 21 days in an incubator with body temperature (+ 37 ° C and 100% humidity). The specimens were placed in a vertical position through a piece of thread that was tied around the root and did not come into

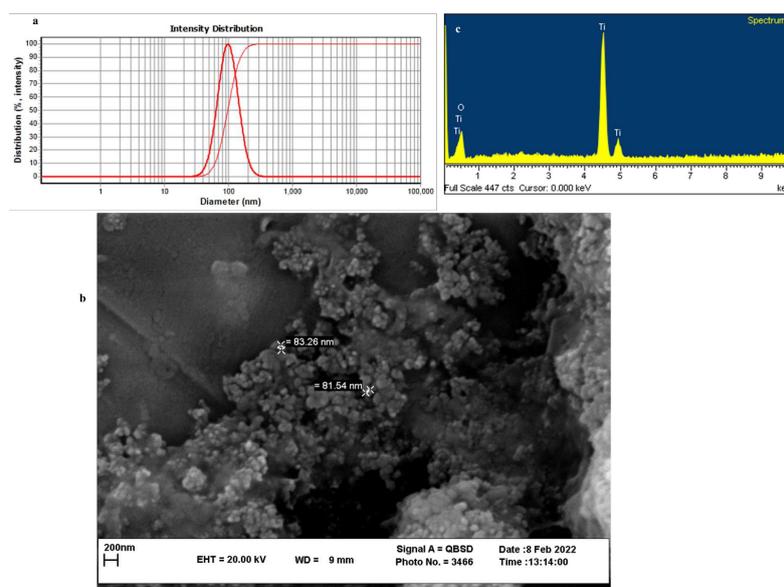


Fig. 1. The morphology of the TiO<sub>2</sub> NPs. a) Dynamic light scattering (DLS), b) Scanning Electron Microscope (SEM) and c) Energy Dispersive X-ray Spectroscopy (EDS)

contact with the crown surfaces so that they were completely immersed in the solution and only in contact with it. This vertical position minimizes the deposition of pigments on the surface of the samples. The samples were washed and brushed with gentle pressure of normal saline solution for one minute every day to be cleaned in case of sediments. Fresh solution was prepared daily and the samples were placed in it.

#### **Evaluate the color of the samples after coloring in coffee solution**

Color evaluation was performed in a similar way to the previous method. The color difference for each group was calculated between the initial assay and the subsequent color change process.  $\Delta L^*$ ,  $\Delta a^*$ ,  $\Delta b^*$  were calculated and the total color change of teeth ( $\Delta E_1$ : color difference of stained samples with their initial color) of each category was calculated as follows:

$$\Delta E^* = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{1/2}$$

#### **Preparation of carboxymethylcellulose gel containing titanium dioxide nanoparticles**

The selected concentrations of the composite containing TiO<sub>2</sub> NPs were 20% and half of that. We added 1600 mg of TiO<sub>2</sub> NPs powder to 6400 mg of CMC powder dissolved in a suitable amount of sterile distilled water and mixed well to make a 20% CMC gel containing TiO<sub>2</sub> NPs. To prepare

CMC gel with a concentration of 10% TiO<sub>2</sub> NPs, we added 2500 mg of pure CMC gel to 2500 mg of CMC gel containing 20% TiO<sub>2</sub> NPs. The viscosity of the gel was checked visually on the tooth to have a consistency that could cover the surface of the tooth and maintain on it.

#### **Determination of the most effective concentration of gels containing TiO<sub>2</sub> nanoparticles**

To obtain the most effective concentration of gel containing TiO<sub>2</sub> nanoparticles, in terms of color change, bleaching with two different concentrations (10% and 20%) was performed on the samples. The concentration of 10% gel was applied on three samples and the concentration of 20% gel was applied on the other three teeth. In each group, the gel was placed on the teeth for 20 min. The samples were washed and stored in normal saline for one week and then the final color of the samples was recorded.

#### **Record teeth color after bleaching and calculate color change**

The color of the teeth was evaluated and  $\Delta E_2$  was calculated using the mentioned formula and its mean for each group was obtained. To determine the most effective concentration we obtained the mean  $\Delta E_2$  in both groups and compared them so found that the 20% concentration was more effective ( $\Delta E_2$  difference should be at least 3.3).

#### **Primary color measurement of main samples**

The primary color of forty eight human premolars without cracks, surface defects, previous restorations, and anomaly (apart from six prototypes) that were extracted for orthodontic purposes were evaluated using a Minolta colorimeter (Konica Minolta model CR-400) and CIE L\*a\*b\* parameters analysis in a similar way to the previous method. The area for color determination was the middle part of the buccal surface of the teeth.

#### **Preparing and coloring the main samples**

Samples were kept in 0.05% chloramine T solution for one week then they were placed in coffee solution for 21 days in an incubator with body temperature (+ 37 ° C and 100% humidity). All samples were placed in a vertical position. They were washed and brushed daily and were placed in fresh coffee solution.

#### **Evaluate the color of the main samples after coloring in coffee solution**

Samples color was recorded after immersion in coffee and  $\Delta E_1$  was calculated.

#### **The process of the bleaching**

The number of samples was forty-eight which was divided into eight groups each containing six which included two control groups and six groups for exposure to TiO<sub>2</sub> NPs with different activation times and methods. Three groups were exposed to 20% carboxymethylcellulose containing titanium dioxide nanoparticles activated by UV-C.

In the first group, the gel contained TiO<sub>2</sub> nanoparticles that was activated with UV-C by hood for 30 min and frequency of 50 Hz. The gel was placed on the buccal surface of the teeth by micro brush for 20 min. Then it was rinsed from the surface of the teeth by gentle pressure of distilled water.

In the second group, the gel containing TiO<sub>2</sub> nanoparticles, which was activated by UV light, was placed on the teeth for 20 min. Afterwards, it was removed from the tooth surface with sterile cotton soaked in distilled water to place fresh gel on the teeth again for 20 min. The teeth of the second group were rinsed under gentle pressure of distilled water to remove the gel from buccal surfaces.

In the third group, the gel containing TiO<sub>2</sub> nanoparticles, which was activated by UV light,

was placed on the teeth for 20 min. Then the gel was removed to place fresh gel on the teeth again for 20 min and it was removed again to apply fresh gel on the surface of the teeth for the third time and after the third interval of 20 min, the teeth of the third group were rinsed.

The other three groups were exposed to CMC containing 20% titanium dioxide nanoparticles activated by blue light of dental Light Cure (Woodpecker LED.B).

In the first group, the gel containing TiO<sub>2</sub> nanoparticles was placed on the buccal surface of the teeth by micro brush and activated for 20 sec by blue light of light-curing device. The gel remained on the teeth for 20 min, then was rinsed from the surface of the teeth.

In the second group, the gel containing TiO<sub>2</sub> nanoparticles was placed on the teeth and activated for 20 sec by blue light of light-curing device. The gel remained on the teeth for 20 min. Then it was wiped from the surface of the teeth and fresh gel was placed on the teeth again and activated for 20 sec by blue light. After the second 20 min, the teeth of the second group were washed to remove the gel.

In the third group, the gel containing TiO<sub>2</sub> nanoparticles was placed on the teeth and activated for 20 sec by blue light of light-curing device. The gel remained on the teeth for 20 min, then it was removed. The fresh gel was placed on the buccal surface of the teeth again and activated for 20 sec by blue light. After the second 20 min, the teeth of the third group were rinsed. For the third time, fresh gel similar to the previous steps was placed on the buccal surface of the teeth and activated for 20 sec by blue light of light-curing device. After the third 20 min interval, the teeth of the third group were rinsed.

In the positive control group, bleaching was performed three times consecutively using 40% hydrogen peroxide gel for 20 min each time. Between each time the fresh gel was placed on buccal surface of the teeth and the previous gel was cleaned with sterile cotton soaked in distilled water. After whitening for the third time, the teeth were washed under gentle pressure of distilled water like other samples. In the negative control group, CMC gel without nanoparticles was placed on the tooth surface for 20 min and then the samples were rinsed.

According to the instructions in the 40% hydrogen peroxide bleaching gel kit, color

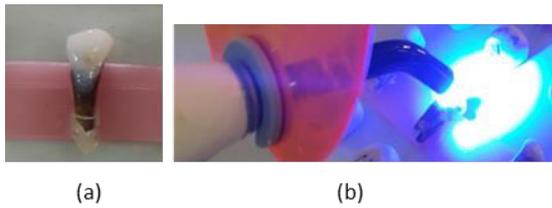


Fig. 2. (a) tooth was whitened by UV-activated CMC gel containing TiO<sub>2</sub> nanoparticles. (b) tooth was whitened by blue light-activated CMC gel containing TiO<sub>2</sub> nanoparticles

measurement of samples was done 48 hours after bleaching.

**Final color measurement of main samples**

Color comparisons were done in a similar way to the previous method by calculating  $\Delta E_2$  (color difference of samples after bleaching compared to the colored state).

**Data analysis**

All data were analyzed using GraphPad Prism 7.0 software (San Diego, CA, USA) and presented as the mean±standard deviation (SD). The differences between groups were analyzed by Student’s t-test and one-way analysis of variance (ANOVA) followed by Tukey’s multiple comparison test. *P* value < 0.05 was set as statistically significant.

**RESULTS**

The size distributions and morphology of the TiO<sub>2</sub> NPs were confirmed via DLS, SEM and EDC and shown in (Fig. 1a-c). SEM image illustrated the spherical shape of the TiO<sub>2</sub> NPs. The particle size of TiO<sub>2</sub> NPs using DLS analysis, as indicated in (Fig. 1 a), showed a size 98±23.

The results for determining the more effective concentration of CMC containing titanium

Table 1. Results of tooth color examination in prototypes after bleaching with two concentration of CMC gel containing TiO<sub>2</sub> NPs (gel exposure time : 20 min).  $\Delta E_1$ : Color difference after staining with coffee compared to the initial tooth color.  $\Delta E_2$ : Color difference after bleaching compared to the color after staining with coffee

Tooth number and concentration	$\Delta E_1$	$\Delta E_2$
Teeth 1 group 10%	6.2468	2.5030
Teeth 2 group 10%	1.7543	2.7071
Teeth 3 group 10%	7.6140	1.3432
Teeth 1 group 20%	12.3709	3.2028
Teeth 2 group 20%	6.5057	4.4631
Teeth 3 group 20%	10.1073	3.4010

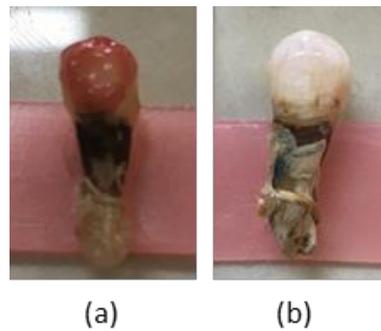


Fig 3. Control groups. (a) tooth was whitened by hydrogen peroxide. (b) tooth was whitened by CMC

dioxide nanoparticles are shown in Table 1. According to the value of  $\Delta E_2$  and compare it between two bleached groups with 10% and 20% concentration of CMC gel containing TiO<sub>2</sub> nanoparticles, 20% concentration of gel was the effective concentration ( $\Delta E_2$  difference should be at least 3.3). Table 2 shows the  $\Delta E_1$  mean in the exposure and control groups. According to the Fig. 4 in the group, once exposed to gel containing UV-activated TiO<sub>2</sub> nanoparticles the  $\Delta E_2$  mean value was 3.83. There was a statistically significant difference in this group compared to the CMC control group with  $\Delta E_2$ :2.54, (*P*≤0.04). Also, in comparison with H<sub>2</sub>O<sub>2</sub> control group with  $\Delta E_2$ : 6.34, the results indicated a significant difference, (*P* ≤0.02) (Fig. 4a). In the group twice exposed to gel containing UV-activated TiO<sub>2</sub> nanoparticles, the  $\Delta E_2$  mean value was 4.19. There was a statistically significant difference in this group compared to CMC control group with  $\Delta E_2$ :2.54, (*P* ≤ 0.05) but with H<sub>2</sub>O<sub>2</sub> control group with  $\Delta E_2$ :6.43 no significant difference was observed (*P* ≤0.064) (Fig. 4b). In the group three times exposed to gel containing UV-activated TiO<sub>2</sub> nanoparticles the  $\Delta E_2$

Table 2. Mean  $\Delta E_1$  of experimental and control groups.  $\Delta E_1$ : Color difference after staining with coffee compared to the initial tooth color

Examination group	Mean $\Delta E_1$
UV activated group one time exposed	6.96
UV activated group two times exposed	8.92
UV activated group three times exposed	10.44
Blue light activated group one time exposed	8.23
Blue light activated group two times exposed	9.01
Blue light activated group three times exposed	8.07
CMC control group	6.19
H <sub>2</sub> O <sub>2</sub> control group	9.61

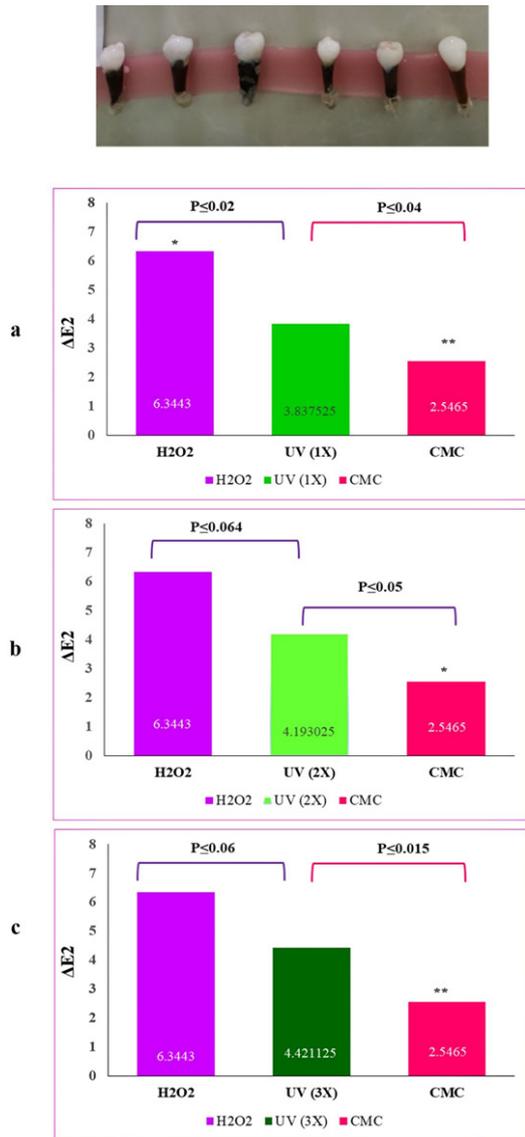


Fig. 4.  $\Delta E_2$  results in groups were exposed to CMC gel containing  $\text{TiO}_2$  nanoparticles that were activated by UV. (a) Color change ( $\Delta E_2$ ) of bleached group with CMC gel containing UV-activated  $\text{TiO}_2$  nanoparticles (UV-C, f: 50 Hz, 30 min) during one time exposure (20 min) compared to control groups. (b) Color change ( $\Delta E_2$ ) of bleached group with CMC gel containing UV-activated  $\text{TiO}_2$  nanoparticles (UV-C, f: 50 Hz, 30 min) during two times exposure (each time 20 minutes) compared to control groups. (c) Color change ( $\Delta E_2$ ) of bleached group with CMC gel containing UV-activated  $\text{TiO}_2$  nanoparticles (UV-C, f: 50 Hz, 30 min) during three times exposure (each time 20 min) compared to control groups

mean value was 4.42. In this group, a statistically significant difference was observed with the CMC control group with  $\Delta E_2$ : 2.54, ( $P \leq 0.015$ ) but compared to the  $\text{H}_2\text{O}_2$  control group with  $\Delta E_2$ : 6.34 no significant difference was observed ( $P \leq 0.06$ ) (Fig. 4c). In the group, once exposure to gel

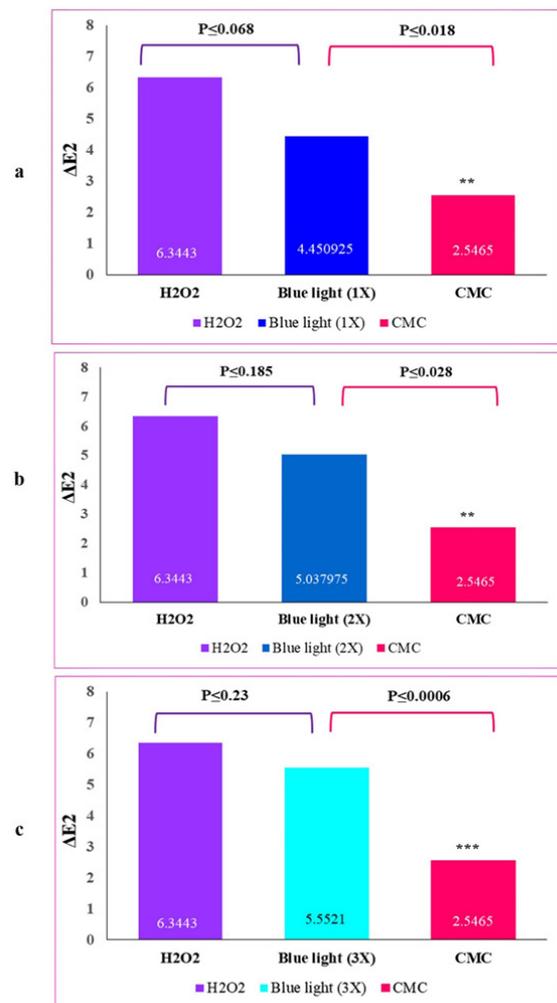


Fig. 5.  $\Delta E_2$  results in groups were exposed to CMC gel containing  $\text{TiO}_2$  nanoparticles that were activated by blue-light. (a) Color change ( $\Delta E_2$ ) of bleached group with CMC gel containing blue-light activated  $\text{TiO}_2$  nanoparticles during one time exposure (light irradiation time: 20 sec, gel exposure time: 20 min) compared to control groups. (b) Color change ( $\Delta E_2$ ) of bleached group with CMC gel containing blue light-activated  $\text{TiO}_2$  nanoparticles during two times exposure (for each time light irradiation: 20 sec, gel exposure : 20 min) compared to control groups. (c) Color change ( $\Delta E_2$ ) of bleached group with CMC gel containing blue light-activated  $\text{TiO}_2$  nanoparticles during three times exposure (for each time light irradiation: 20 sec, gel exposure : 20 min) compared to control groups

containing  $\text{TiO}_2$  nanoparticles activated by blue light  $\Delta E_2$  mean value was 4.45.  $P$ -value analysis showed a significant difference in comparison with the CMC control group with  $\Delta E_2$ : 2.54 ( $P \leq 0.018$ ) but in the hydrogen peroxide control group with  $\Delta E_2$ : 6.34 there was no significant difference ( $P \leq 0.068$ ) (Fig. 5a). In the group twice exposed to gel containing  $\text{TiO}_2$  nanoparticles activated by

blue light with a mean of  $\Delta E_2$ : 5.03 there was a statistically significant difference compared to CMC control group with  $\Delta E_2$ : 2.54 ( $P \leq 0.028$ ) but with hydrogen peroxide control group with  $\Delta E_2$ : 6.43 the difference was not significant ( $P \leq 0.185$ ) (Fig. 5b). In the group three times exposed to gel containing TiO<sub>2</sub> nanoparticles activated by blue light with a mean of  $\Delta E_2$ : 5.55, a significant difference was obtained compared to the CMC control group with  $\Delta E_2$ : 2.54 ( $P \leq 0.0006$ ) but in comparison with H<sub>2</sub>O<sub>2</sub> control group with  $\Delta E_2$ : 6.34 statistical results did not show a significant difference ( $P \leq 0.23$ ) (Fig. 5c). Between six exposure groups, in the group that TiO<sub>2</sub> NPs were activated by blue light higher levels of bleaching was observed and highest value was for the group that was exposed to the gel and activated with blue light, three times. In all groups the bleaching effect of titanium dioxide nanoparticles was less than the hydrogen peroxide control group and the CMC control group didn't have any bleaching effect on samples.

## DISCUSSION

The current in-vitro research compares the effect of titanium dioxide photocatalyst on bleaching with hydrogen peroxide. Currently, most of the in-office bleaching products contain high levels of H<sub>2</sub>O<sub>2</sub> to increase release of free radicals [31]. Based on the reaction condition, H<sub>2</sub>O<sub>2</sub> has the ability to form various reactive oxygen species (ROS), which can remove stains, particularly the hydroxyl radical (OH), because of their decomposition of organic substances [32]. In addition, some novel bleaching approaches are developing, with higher effectiveness. A well-adapted system of a light source and an adequate photocatalytic nanoparticle bleaching gel could allow localized production of reactive oxygen species, including hydrogen peroxide and hydroxyl radicals, and boost the bleaching effect while reducing potential adverse side effects [2]. These are typically semiconducting nanoparticles with a bandgap in the UV or visible light [2]. As a photocatalyst, TiO<sub>2</sub> stimulates a redox reaction and decomposes organic compounds when light-irradiated [33]. TiO<sub>2</sub> absorbs light above bandgap energy and electrons are excited to the conduction band. Such electrons result in declined oxygen level, release of superoxide radicals like (O<sub>2</sub><sup>•-</sup>). Meanwhile, the holes, formed in the valence band, lead to declined level of hydroxide ions and generation of hydroxyl radicals. According to

the evidence, these radicals could discolor tooth-coloring organic compounds by oxidation and degradation [26]. In this method, the production of hydroxyl radicals can be controlled through light radiation, thus reducing side effects. In addition, such compounds are known for their semiconductor photocatalyst reacting to ultraviolet light [34]. When irritated under the UV light, TiO<sub>2</sub> NPs shows photocatalytic properties that result in oxidative destruction of an extensive spectrum of organic compounds [35] and dyes [27, 36]. Nevertheless, TiO<sub>2</sub> can react at visible light exposure of 400 nm vicinity, similar to the wavelength of common light sources administered in dental light-curing units [37]. Increased attention has been paid to the enhanced absorption of TiO<sub>2</sub> and photoactivity in the visible region [38]. Many articles examined the impact of visible light irradiation [22, 37] and irradiation time [37] on the photocatalytic activity of TiO<sub>2</sub> nanoparticles and concluded that both factors affect on photocatalytic activity of nanoparticles. Most of the previous research emphasized the impact of different light sources on bleaching action [34, 37, 39]. LED source produces minimum thermal insult during the light activation stage [40-42] and the side effects caused by it are not long lasting [43]. In this study, titanium dioxide nanoparticles were activated using UV and blue light.

Several in vitro models are developed to assess the efficacy of tooth bleaching products and techniques, which mostly applied whole or cut human or bovine tooth samples in the pre-existing colors. Nevertheless, in some in-vitro models, the level of intrinsic tooth color by pre-staining is enhanced [34]. In this study, we stained human teeth with coffee. In some studies, the bleaching effect of titanium dioxide has been evaluated by sample solution. All studies concluded that titanium dioxide can degrade dyes [15, 22, 27, 36, 44]. Zhang *et al.* introduced that a polydopamine (PDA)-modified titanium dioxide nanoparticles (nano-TiO<sub>2</sub>@PDA) as a new blue-light-activated tooth can also have bleaching effect on the teeth similar to the impact of H<sub>2</sub>O<sub>2</sub>-based whitening agents in clinical [6]. There was a slight difference between the method employed in the recent study and ours. While teeth were initially stained with coffee in our study, Zhang *et al.* did not use the staining step. At high initial concentrations of dye, the photocatalytic activity of TiO<sub>2</sub> nanoparticle decreases [44]. This may be the reason for the

difference between the results of this study and the study [6] that has evaluated blue-light-activated nano-TiO<sub>2</sub>@PDA for highly effective and nondestructive tooth whitening. In this study, all groups (Except the CMC control group) the mean ΔE was more than 3.3 (clinically observable). Also, compared to the two groups activated with blue light and UV, the group activated with blue light had higher bleaching effect in the samples. The best efficiency and effectiveness related to the group of three times exposure to the gel containing titanium dioxide nanoparticles activated by blue light. The reason for the higher effectiveness of groups exposed to blue light than UV, unlike higher UV energy, maybe due to the difference in how the nanoparticles was activated with the mentioned waves. In the UV-activated groups, the prepared gel was UV irradiated once at the beginning of the experiment, then exposed to the samples, and in two and three exposure groups, the same gel was used again on the teeth. This passage of time may have reduced the dye degradation activity of nanoparticles by returning the excited electrons to the previous energy level and the inability to produce hydroxyl radicals, but to activate with blue light, first the gel containing 20% titanium dioxide nanoparticles was placed on the surface of the teeth and then light-cure blue light was shone on each tooth of the desired group for 20 sec. Therefore, by changing the UV irradiation process in 2 and 3 times exposures, it is expected that the performance of UV-activated groups will improve. The results in each group showed that an increase in the frequency of UV and blue light radiation leads to a brighter color of the samples.

## CONCLUSION

Bleaching has become a common method in cosmetic dentistry today so use of bleaching agents is increasing. Several studies and many efforts have been made to achieve an effective and efficient way to whiten teeth in a way that has minimal side effects. In this study, using CMC, a gel containing titanium dioxide nanoparticles was made, which increased the efficiency of nanoparticles in the bleaching process and made its application easier. UV and blue light irradiation was used to activate the nanoparticles. Our results showed visible light had better effect on TiO<sub>2</sub> nanoparticles photocatalytic activity than UV. However, this is due to the difference in how carboxymethylcellulose gel containing titanium

dioxide nanoparticles was activated with both blue light and UV sources. All groups had less whitening effect than the group that whitened with 40% hydrogen peroxide gel. This could be due to severe discoloration of the teeth because of being in coffee for a long time.

## ACKNOWLEDGMENTS

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## CONFLICTS OF INTERESTS

No conflict of interest was reported by the authors.

## REFERENCES

1. Joiner A. The bleaching of teeth: a review of the literature. *J Dent.* 2006;34(7):412-419.
2. Kurzmann C, Verheyen J, Coto M, Kumar RV, Divitini G, Shokoohi-Tabrizi HA, et al. In vitro evaluation of experimental light activated gels for tooth bleaching. *Photochem Photobiol Sci.* 2019;18(5):1009-1019.
3. Affairs ADACoS. Tooth whitening/bleaching: treatment considerations for dentists and their patients. Chicago: ADA. 2009.
4. Mondelli RFL, Francisconi AC, Almeida CMD, Ishikiriama SK. Comparative clinical study of the effectiveness of different dental bleaching methods—two year follow-up. *J Appl Oral Sci.* 2012;20(4):435-443.
5. Hanks C, Fat J, Wataha J, Corcoran J. Cytotoxicity and dentin permeability of carbamide peroxide and hydrogen peroxide vital bleaching materials, *in vitro*. *J Dent Res.* 1993;72(5):931-938.
6. Zhang F, Wu C, Zhou Z, Wang J, Bao W, Dong L, et al. Blue-light-activated nano-TiO<sub>2</sub>@ PDA for highly effective and nondestructive tooth whitening. *ACS Biomater Sci Eng.* 2018;4(8):3072-3077.
7. Buchalla W, Attin T. External bleaching therapy with activation by heat, light or laser—a systematic review. *Dent Mater J.* 2007;23(5):586-596.
8. Marson FC, Sensi LG, Vieira LCC, Araújo E. Clinical evaluation of in-office dental bleaching treatments with and without the use of light-activation sources. *Operative Dentistry.* 2008;33(1):15-22.
9. Bernardon JK, Sartori N, Ballarin A, Perdigão J, Lopes G, Baratieri LN. Clinical performance of vital bleaching techniques. *Oper Dent.* 2010;35(1):3-10.
10. Alomari Q, El Daraa E. A randomized clinical trial of in-office dental bleaching with or without light activation. *Compend Contin Educ Dent.* 2010;11(1):E017-24.
11. Kugel G, Papathanasiou A, Williams 3rd AJ, Anderson C, Ferreira S. Clinical evaluation of chemical and light-activated tooth whitening systems. *Compendium of continuing education in dentistry (Jamesburg, NJ: 1995).* 2006;27(1):54-62.
12. Noruzi S, Vatanchian M, Azimian A, Niroomand A, Salarinia R, Oroojalian F. Silencing SALL-4 Gene by Transfecting Small Interfering RNA with Targeted Aminoglycoside-Carboxyalkyl Polyethylenimine Nano-Polyplexes Reduced Migration of MCF-7 Breast Cancer Cells. *Avicenna J Med Biotechnol.* 2021;13(1):2.

13. Oroojalian F, Orafaee H, Azizi M. Synergistic antibacterial activity of medicinal plants essential oils with biogenic silver nanoparticles. *Nanomed J.* 2017;4(4):237-244.
14. Akhlaghi M, Taebpour M, Sharafaldini M, Javani O, Haghirsadat BF, Oroojalian F, et al. Fabrication, characterization and evaluation of anti-cancer and antibacterial properties of nanosystems containing *Hedera Helix* aqueous extracts. *Nanomed J.* 2021.
15. Cuppini M, Leitune VCB, de SOUZA M, Alves AK, Samuel SMW, Collares FM. In vitro evaluation of visible light-activated titanium dioxide photocatalysis for in-office dental bleaching. *Dent Mater J.* 2019;2017-2199.
16. Dufefoi W, Moniz K, Allen-Vercoe E, Ropers M-H, Walker VK. Impact of food grade and nano-TiO<sub>2</sub> particles on a human intestinal community. *Food Chem Toxicol.* 2017;106:242-249.
17. Ahmed MA, El-Shennawy M, Althomali YM, Omar AA. Effect of titanium dioxide nano particles incorporation on mechanical and physical properties on two different types of acrylic resin denture base. *World J Nano Sci Eng.* 2016;6(3):111-119.
18. Omid M, Malakoutian M, Choolaei M, Oroojalian F, Haghirsadat F, Yazdian F. A Label-Free detection of biomolecules using micromechanical biosensors. *Chinese Phys Lett.* 2013;30(6):068701.
19. Rahimizadeh M, Eshghi H, Shiri A, Ghadamyari Z, Matin MM, Oroojalian F, et al. Fe (HSO<sub>4</sub>)<sub>3</sub> as an efficient catalyst for diazotization and diazo coupling reactions. *J Korean Chem Soc.* 2012;56(6):716-719.
20. Tabari K, Hosseinpour S, Parashos P, Khozestani PK, Rahimi HM. Cytotoxicity of selected nanoparticles on human dental pulp stem cells. *Iran Endod J.* 2017;12(2):137.
21. Rashidi A, Omid M, Choolaei M, Nazarzadeh M, Yadegari A, Haghiersadat F, et al., editors. Electromechanical properties of vertically aligned carbon nanotube. *Adv Mat Res* 2013; Trans Tech Publ.
22. Epling GA, Lin C. Photoassisted bleaching of dyes utilizing TiO<sub>2</sub> and visible light. *Chemosphere.* 2002;46(4):561-570.
23. Vinagre A, Ramos JC, Rebelo C, Basto JF, Messias A, Alberto N, et al. Pulp temperature rise induced by light-emitting diode light-curing units using an ex vivo model. *Materials.* 2019;12(3):411.
24. Kossatz S, Dalanhol A, Cunha T, Loguercio A, Reis A. Effect of light activation on tooth sensitivity after in-office bleaching. *Oper Dent.* 2011;36(3):251-257.
25. Haghi M, Hekmatafshar M, Janipour MB, Gholizadeh SS, Faraz M, Sayyadifar F, et al. Antibacterial effect of TiO<sub>2</sub> nanoparticles on pathogenic strain of *E. coli*. *Int J Adv Biotechnol Res.* 2012;3(3):621-624.
26. Komatsu O, Nishida H, Sekino T, Yamamoto K. Application of titanium dioxide nanotubes to tooth whitening. *Nano biomedicine.* 2014;6(2):63-72.
27. Schneider SL, Lim HW. A review of inorganic UV filters zinc oxide and titanium dioxide. *Photodermatol Photoimmunol Photomed.* 2019;35(6):442-446.
28. Hebeish A, Hashem M, Abd El-Hady M, Sharaf S. Development of CMC hydrogels loaded with silver nanoparticles for medical applications. *Carbohydr Polym.* 2013;92(1):407-413.
29. Benchabane A, Bekkour K. Rheological properties of carboxymethyl cellulose (CMC) solutions. *Colloid Polym Sci.* 2008;286(10):1173.
30. Han S, Wang T, Li B. Preparation of a hydroxyethyl-titanium dioxide-carboxymethyl cellulose hydrogel cage and its effect on the removal of methylene blue. *J Appl Polym Sci.* 2017;134(23).
31. Tano E, Otsuki M, Kato J, Sadr A, Ikeda M, Tagami J. Effects of 405 nm diode laser on titanium oxide bleaching activation. *Photomed Laser Surg.* 2012;30(11):648-654.
32. Martín J, Ovies N, Cisternas P, Fernández E, Junior OO, De Andrade M, et al. Can an LED-laser hybrid light help to decrease hydrogen peroxide concentration while maintaining effectiveness in teeth bleaching? *Laser Phys.* 2015;25(2):025608.
33. Eimar H, Siciliano R, Abdallah M-N, Abi Nader S, Amin WM, Martinez P-P, et al. Hydrogen peroxide whitens teeth by oxidizing the organic structure. *J Dent.* 2012;40:e25-e33.
34. Kishi A, Otsuki M, Sadr A, Ikeda M, Tagami J. Effect of light units on tooth bleaching with visible-light activating titanium dioxide photocatalyst. *Dent Mater J.* 2011;30(5):723-729.
35. Rengifo-Herrera JA, Blanco MN, Pizzio LR. Photocatalytic bleaching of aqueous malachite green solutions by UV-A and blue-light-illuminated TiO<sub>2</sub> spherical nanoparticles modified with tungstophosphoric acid. *Applied Catalysis B: Environmental.* 2011;110:126-132.
36. Al-Dawery SK. Photo-catalyst degradation of tartrazine compound in wastewater using TiO<sub>2</sub> and UV light. *J Eng Sci Technol.* 2013;8(6):683-691.
37. Suyama Y, Otsuki M, Ogisu S, Kishikawa R, Tagami J, Ikeda M, et al. Effects of light sources and visible light-activated titanium dioxide photocatalyst on bleaching. *Dent Mater J.* 2009;28(6):693-699.
38. Mitoraj D, Kisch H, editors. Surface modified titania visible light photocatalyst powders. *Solid State Phenom.* 2010; Trans Tech Publ.
39. Suemori T, Kato J, Nakazawa T, Akashi G, Igarashi A, Hirai Y, et al. Effects of light irradiation on bleaching by a 3.5% hydrogen peroxide solution containing titanium dioxide. *Laser Phys Lett.* 2008;5(5):379.
40. Hofmann N, Hugo B, Klaiber B. Effect of irradiation type (LED or QTH) on photo-activated composite shrinkage strain kinetics, temperature rise, and hardness. *Eur J Oral Sci.* 2002;110(6):471-479.
41. Usumez A, Öztürk N. Temperature increase during resin cement polymerization under a ceramic restoration: effect of type of curing unit. *Int J Prosthodont.* 2004;17(2).
42. Eldeniz AU, Usumez A, Usumez S, Ozturk N. Pulpal temperature rise during light-activated bleaching. *J Biomed Mater Res A / J Biomed Mater Res B Appl Biomater. An Official Journal of The Society for Biomaterials, The Japanese Society for Biomaterials, and The Australian Society for Biomaterials and the Korean Society for Biomaterials.* 2005;72(2):254-259.
43. Oberholzer T, Makofane M, du Preez I, George R. Modern high powered led curing lights and their effect on pulp chamber temperature of bulk and incrementally cured composite resin. *Eur J Prosthodont Restor Dent.* 2012;20(2):50-55.
44. Thomas M, Naikoo GA, Sheikh MUD, Bano M, Khan F. Effective photocatalytic degradation of Congo red dye using alginate/carboxymethyl cellulose/TiO<sub>2</sub> nanocomposite hydrogel under direct sunlight irradiation. *J Photochem Photobiol A Chem.* 2016;327:33-43.