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OPINION
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# Current Status and Future Perspectives of In-office Tooth Bleaching

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## INTRODUCTION

Several chemical components and procedures have been used along the years to resolve dental discolorations (vital and non-vital teeth) (1, 2). However, even though promising bleaching outcomes (3–6) have been reported by numerous studies (*in vitro* and clinical trials), patients typically complain about the occurrence of mild-to-severe post-operatory dentin hypersensitivity (4, 7–9). These concerns have precipitated the execution of extensive studies aiming to improve the safety and efficacy of peroxide-based (hydrogen or carbamide) treatments (10). Despite the widespread clinical acceptance amongst clinicians and patients, and the perceived safety (11) associated with dental bleaching procedures, (12) studies have demonstrated the negative impacts of these so-called minimally invasive and ultraconservative techniques on enamel, (13–15) dentin, pulp and surrounding soft tissues (13, 16–18).

The fundamental mechanism of action associated with peroxide-containing products (hydrogen [HP] or carbamide [CP]) revolves around the generation of reactive oxygen species (ROS) (19). These oxidizing agents such as oxygen, hydroperoxyl, sodium hypochlorite, hydrogen peroxide, ozone and hydroxyl are associated with different redox potentials ($E^0$*, in Volts;* +1.229, +1.510, +1.630, +1.780, +2.075 and +2.800, respectively) (20, 21) and according to Gentil de Moor, (21) the higher the redox potential, the higher the efficacy in breaking conjugated C=C bonds present in large organic molecules (chromophores). The breakage of conjugated bonds results in numerous small-sized molecules that efficiently scatter smaller wavelengths. This physico-chemical process alters the optical behavior of teeth (22) and the visual perception of colors from yellow-brown to bluish-white.

Even though dental bleaching agents have been reported to generate large amounts of ROS, (20) the molecular environment provided by these materials not only limit their transport, from the gel into the crystalline structure, but also hinders the efficacy of these highly reactive and short-lived species. The most common approaches to overcome these limiting factors include the utilization of high concentrations of HP (30–44%), long exposure times to CP (21 days, at-home) or the utilization of external energy sources (heat or visible light). Several light sources have been used with the purpose of improving the efficacy of bleaching procedures and to shorten the exposure of tissues (soft and mineralized) to highly caustic and oxidative agents (23, 24).

Despite the feasibility of the process, numerous reports have indicated that bleaching protocols modulated by visible light render esthetic outcomes that are only similar to those attained by at-home bleaching techniques, thereby questioning the need for the utilization of visible light (25–27). Therefore, this brief opinion article aims to contribute with information regarding the state of the art, recent developments and future perspectives in the field of dental bleaching.

## PAST, PRESENT AND FUTURE OF DENTAL BLEACHING

The first attempt to improve the efficacy of hydrogen peroxide was based on the delivery of thermal energy onto the tooth structure by means of a heated spatula (28, 29). Although, the process provided with excellent esthetic results, the inability to control the diffusion of heat, and the occurrence of irreversible damage to the dentin-pulp complex restricted its widespread utilization. Subsequent developments focused on the utilization of chemical catalysts (oxalic acid) to improve the speed of the reaction and reduce the incidence of adverse effects (1). However, clinical results were associated with intense dentin hypersensitivity that could only be resolved by radical endodontic treatment.

The introduction of visible light in dental bleaching techniques started with light curing units containing quartz-tungsten halogen filament lamps. These devices emit a broad range of wavelengths (between 400 and 525 nm) (30) and tremendous amount of radiant heat (infrared) that must be filtered using band-pass optical filters. In this energy-transfer model, a colored bleaching gel is used to insulate teeth and convert photons into thermal energy. The rationale behind this approach is to raise the temperature of the gel, favor the dissociation of HP and improve the molecular mobility of ROS. Even though studies demonstrated that esthetic results were better than those attained with at-home bleaching techniques, high levels of dentin hypersensitivity were still being reported by treated patients (31).

Light-emitting diodes (LEDs), which are narrow-band and heat-free sources have also been used in in-office dental bleaching procedures. Despite the lower levels of dentin hypersensitivity reported, clinical outcomes were considered poor and were inferior to those from at-home bleaching techniques, which further strengthened the controversy regarding the utilization of visible light. Esteban Florez et al. (22, 28) while investigating the scientific basis of in-office power bleaching procedures, suggested that a photonic catalysis model should be used to improve bleaching outcomes when using heat-free light sources. In the model proposed, visible light irradiation is used to increase chromophores' degree of freedom and create a molecular environment that improves the reactivity of ROS and the breakage of chromophores.

A few clinical studies have investigated the effects of hybrid irradiation (infrared and visible, $780 \pm 5$ nm and $457 \pm 15$ nm, respectively) on the efficacy of in-office bleaching protocols using gels containing 6% of HP (32–34). Even though the hybrid irradiation investigated was shown to enhance the efficacy of bleaching gels with low concentrations of HP, results reported have indicated that bleaching outcomes were still inferior to those of 35% HP. According to those studies, the major benefit of the hybrid irradiation technology (LASER/LED) precipitated from the intrinsic biostimulation properties of low intensity level laser that decreased the incidence, intensity and duration of post-operatory dentin hypersensitivity, (35) thereby positively impacting patient's overall experience and comfort (36).

Photonic bleaching techniques are those that do not use any type of peroxide-containing products, (37–39) and have been suggested as an alternative to resolve dental discolorations without the occurrence of adverse side effects (40). In this pain-free approach, (40) visible radiation of adequate wavelength ($405 \pm 15$ nm) and photon energy (3.06 $\mu$eV) (41) is used to break conjugated C=C and alter the optical behavior of teeth (42, 43). However, even though such photophysical process is feasible from the electronic standpoint, the limited penetration of near-UV wavelengths (44) associated with the desiccation of the crystalline structure, not only decreases the total amount of energy available to permanently break conjugated C=C double bonds, but also eliminates the chances for the generation of ROS. In combination, these factors are clinically translated into less-than-optimal bleaching outcomes and poor chromatic stability (days to weeks) (18, 45–47).

Other studies focused on the incorporation of calcinated metaloxide nanoparticles, such as nitrogen-doped titanium dioxide ($TiO_2$-N), into commercially-available bleaching gels containing hydrogen peroxide (6 to 35%) (36, 48, 49). According to results reported, nanoparticles used behave as semi-conductors and efficiently convert photons into thermal energy (36). Randomized clinical trials have indicated that bleaching techniques modulated by experimental gels containing varying concentrations of HP and $TiO_2$-N, did not result in bleaching outcomes that were better than those attained with unaltered bleaching gels under the same light irradiation conditions (36). Despite all efforts from the manufacturing and scientific communities, bleaching materials and equipment developed were not capable of vertically advancing the field.

This scenario exposes a critical need for novel materials and techniques that are capable of delivering excellent esthetic outcomes without negatively impacting the properties of teeth (surface, mechanical, chemical and biological). Recent studies (50–52) have demonstrated the synthesis of third-generation titanium dioxide nanoparticles co-doped with nitrogen and fluorine ($NF\_TiO_2$, 6–15 nm) using robust and highly reproducible solvothermal reactions. According to Huo et al. (53) the synthetic route reported renders nanoparticles that are highly crystalline, have well-defined pore-size distributions, are electron-deficient, generate substantial amounts of ROS, and display strong antibacterial properties (light and dark conditions) against non-disrupted *Streptococcus mutans* biofilms when functionalized in a commercially-available 5th generation dental adhesive resin (50). These findings are fundamentally important for subsequent developments in the field, because third-generation and visible-light responsive $NF\_TiO_2$ can be easily functionalized into polymers currently used in dental bleaching products (at-home and in-office). If successful, this approach may result in a novel generation of bleaching gels with low concentrations of HP and $NF\_TiO_2$ (lower than 10% HP) that are highly effective, less aggressive to the crystalline structure, and may display important teeth mineralization properties (biomimetic functionalities).

## DISCUSSION

It is clear from a simple review of the literature that significant amount of time, funds and effort have been invested by both the manufacturing and scientific communities to improve the efficacy and safety of dental bleaching procedures. Despite all efforts, in-office dental bleaching techniques modulated by visible light radiation (from heat-free sources) and HP continue to be associated with dentin hypersensitivity, (11) and negative impacts on the properties of teeth (surface, mechanical, chemical and biological) (13, 16–18, 25, 35, 54).

Since dentin hypersensitivity has a strong and positive correlation with the concentration of HP, (55) photonic bleaching approaches have been proposed as a safe, pain- and peroxide-free alternative to resolve light-to-mild dental discolorations in vital teeth. However, even though some reports have demonstrated promising immediate results, (37) the vast majority of the literature has indicated that clinical outcomes are poor and unstable. In fact, a recent study (44) has shown that 98% of the energy delivered onto the enamel (thickness of 1.0 mm) is significantly attenuated when using near-UV wavelengths (∼405 nm), and results in doses of energy (at the enamel-dentin junction) that are below the threshold required to permanently break conjugated double bonds present in chromophores.

This behavior not only results in poor esthetic outcomes, but also in clinical protocols that are longer (in terms of clinical sessions). Based on the context provided, it is our opinion that light irradiation continues to be fundamentally important to improve the efficacy of peroxide-containing products (either HP or CP). It is important to underscore that bleaching protocols modulated by HP and near-UV wavelengths (∼405 nm) result in bleaching outcomes that are superior than those precipitating from the combination between HP and visible light (∼457 nm), (55) thereby indicating a wavelength-dependent mechanism. Two recent randomized clinical trials (56, 57) have corroborated our opinion by demonstrating that bleaching protocols modulated by near-UV radiation and CP resulted in esthetic outcomes that were comparable to those of 35% HP, were long-lasting (up to 1 year), were associated with lower levels of dentin hypersensitivity and clinical sessions that were significantly shorter (∼30 min/each) (56–58).

Subsequent developments in the field should focus on improving the molecular environment of polymers to optimize the generation, transport and penetration of ROS while decreasing HP concentrations used. One possible alternative is the utilization of third-generation and visible light-responsive nitrogen and fluorine co-doped titanium dioxide nanoparticles (NF_$TiO_2$) that are capable of generating substantial amounts of ROS and display strong antibacterial, biomimetic and biocompatibility properties (51, 52, 59). In addition, the development of improved interfacial chemistries for superior functionalization, loading and dispersion of metaloxide nanoparticles in dental polymers is expected to result in stable colloidal sols displaying superior rheological and wettability properties.

Bleaching protocols modulated by visible light radiation and nano-filled bleaching gels may not only display promising esthetic outcomes and low levels of dentin hypersensitivity, but could also display biomimetic properties. In combination, these properties are anticipated to protect the chemical make-up of treated teeth through an ion-exchange mechanism and will have the potential to render treated enamel less soluble to organic acids, thereby adding an additional therapeutic value (biomimetic properties) to dental bleaching treatments. Therefore, subsequent studies in the field should be based on mechanistic methodologies capable of elucidating the processes governing the generation and transport of ROS and the impact of polymer compositions on the efficacy of bleaching procedures.

## AUTHOR CONTRIBUTIONS

MK, PM, and RC searched the literature and wrote the initial draft. FE and VC edited the draft. VC conceptualized and supervised the article. All authors contributed to the article and approved the submitted version.

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