# REVIEW ARTICLE BLEACHING, THE BIOLOGIC ASPECTS -A REVIEW

#### **ABSTRACT:**

Present tooth-bleaching techniques are based upon hydrogen peroxide as the active ingredient. It is applied directly, or produced in a chemical reaction from sodium perborate or carbamide peroxide. Among the successfully bleached teeth 10 to 40% require repeated bleaching. Cervical root resorption is a possible consequence of internal bleaching and is more frequently observed in teeth treated with the thermocatalytic procedure. Tooth sensitivity is a common side-effect of external tooth bleaching. A selective use of tooth bleaching based on high ethical standards and professional judgement is preferred to reduce complications. The purpose of this paper was to critically evaluate the biologic aspects of tooth bleaching.

Keywords: Toxicity, esthetics, bleaching.

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#### INTRODUCTION

In the last decades, tooth whitening or bleaching has become one of the most popular esthetic dental treatments. Although published studies tend to suggest that bleaching is a relatively safe procedure, investigators continue to report adverse effects on hard tissue, soft tissue, and restorative materials. Concerns regarding the safety of all bleaching treatments and products have long existed, but were heightened since the introduction of at-home bleaching.<sup>(1)</sup>

A variety of peroxide compounds, including carbamide peroxide, hydrogen peroxide ( $H_2O_2$ ), sodium perborate and calcium peroxide, have been used as active ingredients for bleaching materials.

#### HISTORY

Bleaching of discoloured, pulpless teeth was first described in 1864, and a verity of materials such as sodium hypochlorite (NaOCl), sodium perborate and H<sub>2</sub>O<sub>2</sub> has been used, alone, in combination, and with and without heat activation<sup>(2)</sup>. "Walking bleach" technique that was introduced in 1961 involved the placement of a mixture of sodium perborate and water into the pulp chamber that was sealed off between the patient's visits to a clinician.<sup>(3)</sup> The method was later modified and water was replaced by 30-35% H<sub>2</sub>O<sub>2</sub>, to improve the whitening effect<sup>(4)</sup>. The observation that carbamide peroxide caused lightening of the teeth was made in the late1960s by an orthodontist who had prescribed an antiseptic containing 10% carbamide peroxide to be used in a tray for the treatment of gingivitis<sup>(5)</sup>.

#### SAFETY CONCERNS

Free radicals, that are produced by the peroxides are known to be capable of reacting with proteins, lipids and nucleic acids, causing cellular damage. Because of the potential of  $H_2O_2$  to interact with DNA, concerns with carcinogenicity and co-carcinogenicity of hydrogen peroxide have been raised, although these concerns so far have not been substantiated through research<sup>(6,7,8)</sup>.

Similar to other dental and medical interventions, questions have been raised about the safety of tooth whitening treatments during pregnancy. In the absence of such evidence, clinicians may consider recommending that a tooth whitening be deferred during pregnancy.

The safety of tooth bleaching for children and adolescents is also a consideration. If possible, delaying treatment until after permanent teeth have erupted is recommended, as is use of a custom-fabricated bleaching tray to limit the amount of bleaching gel<sup>(9)</sup>. Close professional and parental/guardian supervision are needed to maximize benefits and minimize adverse effects and overuse.

A "bleaching light" is sometimes used with in-office bleaching procedures. Reports suggest that pulpal temperature can increase with bleaching light use, depending on the light source and exposure time. Pulpal irritation and tooth sensitivity are higher with use of bleaching lights or heat application, and caution has been advised with their use.

However, studies have shown that  $H_2O_2$  is an irritant and also cytotoxic. It is known that a concentrations of 10%  $H_2O_2$  or higher, the chemical is potentially corrosive to mucous membranes or skin, and can cause a burning sensation and tissue damage<sup>(6,10)</sup>. The amount of products applied during office bleaching treatment and other formulation variables can change the potential to cause damage.

#### **MECHANISM OF BLEACHING**

The colour producing materials in solution or on a surface are typically organic compounds that possess extended conjugated chains of alternating single or double bonds and often include heteroatoms, carbonyl, and phenyl rings in the conjugated system and are often referred to as a chromophore. Bleaching and decolouration of the chromophore can occur by destroying one or more of the double bonds in the conjugated chain, or by oxidation of other chemical moieties in the conjugated chain<sup>(11)</sup>.

 $\rm H_2O_2$  oxidises a wide variety of organic or inorganic compounds. The mechanisms of these reactions are varied and dependent on the substrate, the reaction environment, and catalysis. In general, the mechanism of bleaching by  $\rm H_2O_2$  is not well understood and it can form a number of different active oxygen species depending on reaction conditions, including

77

temperature, pH, light and presence of transition metals<sup>(12)</sup>.

Under alkaline conditions,  $H_2O_2$  bleaching generally proceeds via the perhydroxyl anion (HO<sub>2</sub>). Other conditions can give rise to free radical formation, for example, by haemolytic cleavage of either an O-H bond or the O-O bond in  $H_2O_2$  to give  $H^0 + {}^0OOH$  and  $2^0OH$  (hydroxyl radical), respectively<sup>12</sup>. Under photochemically initiated reactions using light or lasers, the formation of hydroxyl radicals from  $H_2O_2$  has been shown to increase<sup>(13)</sup>.

As peroxide diffuses into the tooth, it can react with organic coloured materials found within the tooth structures leading to reduction in colour<sup>(14)</sup>. For tetracycline stained teeth, the colour is derived from photo-oxidation of tetracycline molecules bound within the tooth structures<sup>(15)</sup>. The mechanism by which peroxide affects the tetracycline stain is considered to be by chemical degradation of the unsaturated quinone type structures found in tetracycline leading to less coloured molecules<sup>(16,17)</sup>.

#### **ADVERSE EFFECTS**

Cervical root resorption is an inflammatorymediated external resorption of the root, which can be seen after trauma and following intracoronal bleaching<sup>(18)</sup>. A high concentration of  $H_2O_2$  in combination with heating seemed to promote cervical root resorption<sup>(18,19)</sup>. The underlying mechanism for this effect is unclear, but it has been suggested that the bleaching agent reaches the periodontal tissue through dentinal tubules and initiates an inflammatory reaction<sup>(20)</sup>. It has also been speculated that the peroxide, by diffusing through the dentinal tubules, dentures the dentin, which then becomes an immunologically different tissue and is attacked as a foreign body<sup>(21)</sup>. Frequently, the resorption was diagnosed several years after the bleaching<sup>(19,21)</sup>. Invitro studies using extracted teeth showed that H<sub>2</sub>O<sub>2</sub> placed in the pulp chamber penetrated the dentin<sup>(22)</sup> and that heat increased the penetration<sup>(23)</sup></sup>. H<sub>2</sub>O<sub>2</sub> also increased dentin permeability<sup>(24)</sup>, and that may enhance the effects of H<sub>2</sub>O<sub>2</sub> following repeated exposures. Based on the cited literature, the use of a thermo-catalytic bleaching procedure in teeth with cervical defects of the cementum constitutes a risk

factor for the development of cervical defects of the cementum constitutes a risk factor for the development constitutes a risk factor for the development of cervical resorption.

Tooth crown fracture has also been observed after intracoronal bleaching, most probably due to extensive removal of the intracoronal dentin. In addition, intracoronal bleaching with  $H_2O_2$ , has been found to reduce the micro-hardness of dentin and enamel<sup>(25)</sup> and weaken the mechanical properties of dentin<sup>(26)</sup>.

#### LOCAL SIDE EFFECTS

#### A - Tooth sensitivity

Tooth sensitivity is a common side-effect of external tooth bleaching. Higher incidence of tooth sensitivity (from 67 to 78%) was reported after in-office bleaching with  $H_2O_2$  in combination with heat. Tooth sensitivity normally persists for up to 4 days after the cessation of bleaching treatment, but a longer duration of up to 39 days has been reported.

The mechanisms that would account for the tooth sensitivity after external tooth bleaching have not yet been fully established. Invitro experiments have shown that peroxide penetrated enamel and dentin and entered the pulp chamber<sup>(27)</sup>, and that the penetration of restored teeth was higher than that of intact teeth. The amount of peroxide detected in the pulp chamber was related to the concentration of  $H_2O_2$  in the preparations applied<sup>(28)</sup>, and also varied among different brands of bleaching agents with the same declared concentration of carbamide peroxide<sup>(27)</sup>. The concentration of peroxide in the pulp chamber was not determined in the above studies, and the clinical significance of the findings is therefore unclear.

Tooth sensitivity was also a common symptom in patients who had not bleached their teeth, and their symptom was correlated with gingival recession<sup>(29)</sup>. Patients with a previous history of tooth sensitivity may thus have a higher risk for such an adverse effect from external tooth bleaching, and this should be taken into account before treatment begins.

#### B-Mucosal irritation

A high concentration of  $H_2O_2$  (from 30 to 35%) is caustic to mucous membranes and may cause burns

and bleaching of the gingiva. In clinical trials that used 10% carbamide peroxide in custom-made trays, from 25 to 40% of the patients reported gingival irritation during treatment. It is therefore advisable that the tray be designed to prevent gingival exposure by the use of a firm tray that has contact with solely the teeth. In this respect, bleaching strips may be unfavourable, since the bleaching gel will come into contact with the gingiva.

#### C-Alteration of enamel surface

Morphological alteration of enamel following tooth bleaching has been addressed in several studies. By infrared spectroscopic analysis, it was found that in vitro treatment of extracted teeth with 35% carbamide peroxide for 30 min/day for 4 days changed the inorganic composition of the enamel, whereas 10% and 16% concentrations did not<sup>(30)</sup>. A high concentration of carbamide peroxide was detrimental to enamel surface integrity, but the damage was less than that seen after phosphoric acid etch. A clinical implication of these findings may be that the teeth are more susceptible to extrinsic discolouration after bleaching due to increased surface roughness.

#### D - Effects on restorations

Data from laboratory studies documented, increased mercury release from dental amalgams exposed to carbamide peroxide solutions for periods ranging from 8 hours to 14-28 days. The amount of mercury released varied with type of amalgam and type of bleaching agent and ranged from 4 times to 30 times higher than in saline controls. It has been suggested that the bleaching may increase the solubility of glass ionomer and other cements. Furthermore, the bond strength between enamel and resin-based fillings was reduced in the first 24 hours after bleaching. After 24 hours, there was no difference in the strengths of dental composite resin cement bonds to bleached and non-bleached enamel<sup>(31)</sup>. Following bleaching, H<sub>2</sub>O<sub>2</sub> residuals in the enamel inhibit the polymerization of resin-based materials and thus reduce bond strength<sup>(32)</sup>. Therefore, tooth-bleaching agents should not be used prior to restorative treatment with resin-based materials.

#### GENOTOXICITY

#### AND CARCINOGENICITY

The genotoxicity of H<sub>2</sub>O<sub>2</sub> and of tooth whiteners containing carbamide peroxide has been evaluated<sup>(33)</sup>. The consensus arising from these evaluations was the direct contact with H<sub>2</sub>O<sub>2</sub> induced genotoxic effects in bacteria and cultured cells. When H<sub>2</sub>O<sub>2</sub> was administered to bacteria or cultured cells in the presence of catalase or other metabolizing enzymes, the effect was reduced or abolished. Since the hydroxyl radicals, perhydroxyl ions, and superoxide anions formed from H<sub>2</sub>O<sub>2</sub> are capable of attacking DNA, the genotoxic potential of H<sub>2</sub>O<sub>2</sub> is dependent on the accessibility of free radicals to target DNA. This may explain why H<sub>2</sub>O<sub>2</sub> induces genotoxicity in the presence of metabolizing enzymes neither in vitro nor in vivo. Tooth whiteners containing carbamide peroxide were mutagenic in certain bacterial strains and non-mutagenic in the presence of additional activating enzymes.

The International Agency for Research on Cancer (IARC) concluded that there is limited evidence in experimental animals and inadequate evidence in humans for the carcinogenicity of  $H_2O_2$  and classified the chemical into Group 3: Unclassifiable as to carcinogenicity to humans<sup>(34)</sup>. The genotoxicity of  $H_2O_2$  in oral health products has been evaluated by The Scientific Committee on Cosmetic Products and Non-Food Products. It appears unlikely that oral health products containing or releasing  $H_2O_2$  up to 3.6%  $H_2O_2$  will enhance cancer risk in individuals except in those who have an increased risk of oral cancer due to tobacco use, alcohol abuse, or genetic predisposition.

### TOXICITY OF HYDROGEN PEROXIDE AND CARBAMIDE PEROXIDE DUE TO HUMAN EXPOSURE

The acute effects of  $H_2O_2$  ingestion are dependent of the amount ingested and the concentration of the  $H_2O_2$  solution. The outcomes of accidental ingestion, or intentional ingestion for suicide, of solutions of 10%  $H_2O_2$  and higher were more severe than those seen at lower concentrations accidental ingestion of 35%  $H_2O_2$  has resulted in several fatal or near-fatal poisionings. In children ingestion of  $H_2O_2$  and

79

carbamide peroxide produce ulceration of the oral mucosa, esophagus, and stomach, accompanied by symptoms such as nausea, vomiting, abdominal distention, and sore throat. It is therefore important to keep syringes with bleaching agents out of the reach of children, to prevent any possible accident<sup>3</sup>.

# RISK ASSESSMENT OF TOOTH BLEACHING

Risk assessment is traditionally considered to consist of 4 steps: the hazard identification, the doseresponse relationship, the exposure assessment, and the risk characterization. The risk characterization is founded on critical comparison of the data on exposure and the dose-response relationship. The amount of bleaching agent used for bleaching one arch of teeth has been calculated to be 900 mg per application when administered according to the manufacturer's instruction<sup>(36)</sup>, and an average of 500 mg per application based on clinical experiments. At least 25% of the bleaching agent administered in bleaching trays is ingested during 2 hours of bleaching<sup>(37)</sup>. This safety factor is not reached in preparations that deliver or contain more than 12.6% H<sub>2</sub>O<sub>2</sub> when 500 mg of bleaching agent is used for bleaching one arch.

Longer bleaching periods per day, multiple applications, bleaching maxillary and mandibular teeth at the same time, and overfilling the tray increase the exposure and reduce the safety factor. For example, if both maxillary and mandibular teeth are bleached at the same time, the minimum required safety factor will not be reached for preparations that contain or deliver more than 7.9% H<sub>2</sub>O<sub>2</sub>, which corresponds to 22% carbamide peroxide. According to the exposure data from a previous evaluation (900 mg/application)  $^{(36)}$ , the concentration of  $H_2O_2$  should not exceed 3.5%, which correspond to 10% carbamide peroxide. Based on the risk assessment, it must be concluded that selection of preparations with a low concentration of carbamide peroxide is recommended for the optimum safety of the patient. In addition, overfilling the tray without removing excess material, biting on the tray, and bleaching both maxillary and mandibular teeth at the same time are not advisable.

#### CONCLUSION

Tooth bleaching is one of the most conservative and cost-effective dental treatments to improve or enhance a person's smile. However, tooth bleaching is not risk-free and only limited long-term clinical data are available on the side effects of tooth bleaching. Accordingly, tooth bleaching is best performed under professional supervision and following a pretreatment dental examination and diagnosis.

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