Republic of Iraq
Ministry of Higher Education
and Scientific Research
University of Baghdad
College of Dentistry

Adverse effects of vital teeth bleaching

A Project Submitted to
The College of Dentistry, University of Baghdad, Department of Oral histology
in Partial Fulfillment for the Bachelor of Dental Surgery

By

Salah mohammed abed

Supervised by:

Assist. Lec. Rusul Jaffar Hadi

B.D.S., M.Sc. (Oral Histology)

2022 A.D. **1443 A.H.**

Certification of the Supervisor

I certify that this project entitled **" Adverse effects of vital teeth bleaching"** was prepared by **Salah mohammed abed** under my supervision at the College of Dentistry / University of Baghdad in partial fulfillment of the graduation requirements for the **B.D.S. degree**.

The supervisor

Assist. Lec. Rusul Jaffar Hadi

B.D.S., M.Sc.(Oral Histology)

Dedication

To my heart family who stand with me at every step and never let me alone till this moment of my life and have the most role in my success, they gave me the power to stay strong and never fall down.

To my father, I want to tell him that I did it, I promise him that I will make him proud of me, thank you for all you have done throughout my life, you raised me, protected me and taught me all you know.

To my all friends thank you for being by my side today and always. Finally to my supervisor who encourage me to keep going on in my study life.

Acknowledgment

Thanks Allah for everything, for providing me with power and patience to perform this study. I would like to express grateful thanks to dean of college of dentistry, University of Baghdad **Prof. Dr. Raghad A. Al-Hashimi.** Grateful thanks are expressed to **Prof. Dr. Bashar Hamid Abdullah** head of department of oral diagnosis for his scientific support and advice.

To my supervisor **Assist. Lec. Rusul Jaffar Hadi**, I would like to express gratitude to scientific care and to the spirit of high morality that encourage and advise me always to right way throughout this research Ask Allah to reward her the best reward. Great thanks to all members of Oral Histology Department for high ethics and for standing help.

Thanks everyone who helped me in the completion of the search for scientific truth. Finally I would like to express grateful thanks to my lovely family, my wonderful parents

List of contents

List of figures

List of Abbreviations

Abbreviation	Phrase
H2O2	Hydrogen peroxide
OTC	Over-the-counter
CP	Carbamide peroxide
ROS	Reactive oxygen species
NaBO3	Sodium perborate
ClO2	Chlorine dioxide
ACP	Amorphous Calcium phosphate
HP	Hydrogen peroxide
SEM	scanning electron microscopy
SOD	superoxide dismutases
SioO2	silicon dioxide
K2O2	potassium peroxide

Introduction

Teeth whitening or teeth bleaching is a procedure which represents the most traditional way to modify the color of teeth. Whitening is often desirable when teeth become yellowed over time for a number of reasons. Hydrogen peroxide (H2O2) is the active ingredient most commonly used in whitening products and is delivered as either hydrogen peroxide or carbamide peroxide. **(Pontes *et al.*, 2020).**

Hydrogen peroxide is analogous to carbamide peroxide as it is released when the stable complex is in contact with water. The hydrogen peroxide (H2O2) act as a dental oxidizing agent which breakdown the colouring substances (chromogens) within or on the tooth resulting in effective color change (**Clifton, 2014).**

There are three essential methods regarding to bleaching of the vital teeth include in-office (power bleaching), at-home (dentist supervised night-guard bleaching), and bleaching with over-the-counter (OTC) products **(Goldberg *et al*., 2010).**

The advantages of tooth bleaching such as preservation of tooth structure, lower cost and satisfactory cosmetic results have been reported, however, the hydrogen peroxide can results in different adverse effects in the tooth structure by diffusion of its degradation through enamel, dentin reaching the dental pulp. These adverse effects include irritation of the soft tissues, dental hypersensitivity, changes in the structure of the enamel, dentine, restorative materials surfaces and changes in the pulp tissue **(Karaarslan *et al*., 2019).**

Review of Literature

1.1 Tooth staining

According to the Glossary of Prosthodontic Terms, ‘‘stain’’ has been defined as the “discoloration of a tooth surface or surfaces as a result of ingested materials, bacterial action, tobacco, and/or other substances” **(The Glossary of Prosthodontic Terms, 2017).**

There are three categories for tooth discoloration as extrinsic, intrinsic and later presented a third category called internalized discoloration **(Kapadia and Jain, 2018)**. Regarding Intrinsic stains, there are several conditions can cause this type of stain such as: amelogenesis imperfecta, dentinogenesis imperfecta, fluorosis, enamel hypoplasia, tetracycline staining, root resorption and aging **(Sulieman, 2005)**.

Extrinsic stains can be classified as non-metallic and metallic stains. The non-metallic stains are absorbed by acquired pellicle or plaque on the tooth surface **(Prathap *et al.*, 2013**). Metallic stains are might be related to occupational contact to metallic salts or by a number of medicines involving metal salts **(Kapadia and Jain, 2018).**

The third category which is Internalized discoloration can be caused by defect on tooth surface which allows the chromogenic bacteria to enter the tooth and finally leading to staining. There are three types of defects including developmental defects which also cause intrinsic staining (enamel hypoplasia, fluorosis), acquired defects (attrition, abrasion, and erosion) and defects from restorative materials like amalgam causing tooth staining due to the movement of tin into dentinal tubules **(Sulieman, 2005; Mortazavi, 2014).**

Tooth discoloration can be treated by different treatment methods including bleaching **(Majeed *et al*., 2015**), enamel microabrasion **(Pini *et al*., 2015)** and porcelain veneers **(Kanokrungsee and Leevailoj, 2014).** These treatment modalities may be used individually or in combination according to the etiology and degree of the staining **(Kapadia and Jain, 2018).**

1.2 Definition of vital teeth bleaching

The vital teeth bleaching is a treatment used to reestablish the actual natural color of vital teeth or to achieve a whiter color and represents a popular treatment in dentistry. The dental bleaching is oxidizing agent, mainly composing from hydrogen peroxide (H2O2) remove the coloring substances by penetration through the dental enamel and dentin (**Casado *et al*., 2018)**.

The American Dental Association established guidelines for the approval of bleaching products. "Peroxide-containing tooth whitening products are classified into three categories: professional in-office agents, professionally supervised agents for use by patients (at- home), and over-the counter (OTC) bleaching products" **(Kihn, 2007).**

There are different forms of peroxide, such as hydrogen peroxide, carbamide peroxide, sodium perborate,and chlorine dioxide and vary in their methods of application and available in different products such as gels in trays, films ,strips, or paint-on gels, all of them have been revealed to be appropriate methods **(Nadhum and Al-Khafaji, 2014).**

For at-home bleaching, the recommendations reveal by using a low concentration of bleaching agent (10-21% carbamide peroxide). With regard to in office bleaching, hydrogen peroxide concentration is range from (25-

40%) while over-the counter (OTC) bleaching products hydrogen peroxide concentration is range from (3-6%) **(Vaz *et al*., 2016).**

1.2.1 Mechanism of action of dental bleaching agent

Stains are classically composing of organic compounds that possess prolonged chains of alternating single or double bonds and are referred to chromophores. The action of bleaching technique is characterized by chemical degradation of the chromophores **(Carey, 2014; Joshi, 2016).**

The active ingredient in vital tooth bleaching is hydrogen peroxide (H2O2), which is usually delivered in commercial agents as hydrogen peroxide (H2O2) or Carbamide peroxide (CP). CP is a stable complex but when contacts with water break down and release H2O2 and urea. Three distinctive phases can be recognized bleaching method (Diffusion, Interaction, Surface change and color) **(Alqahtani, 2014; Kwon and Wertz, 2015).**

1- Diffusion

In the first phase H2O2 with aid of an activator (chemical or physical) dissociates into hydroxyl radical, hydroperoxyl radical anion, hydroperoxyl radical, superoxide radical anions, and superoxide radical cations. These free radicles called reactive oxygen species (ROS) have a low molecular weight and capable of penetrate through the interprismatic spaces in the enamel and through the dentinal tubules in dentin to interact with the organic chromophores **(Kwon *et al*., 2002).**

Generally, hydrogen peroxide dissociation and penetration had been found to be enhanced according to different factors including: higher hydrogen peroxide concentrations, prolonged application, increased temperature, in young teeth where have larger sizes of the dentinal tubules than older teeth, the tooth with restorations, acidic pH and light activation **(Xu and whang, 2011; Patri *et al*., 2013; Kwon and Wertz 2015).**

2- Interaction

The second phase is involved generally from the interactions of H2O2 degradation with the organic chromophores and this interaction named as the "Chromophore Theory''. There are different factors influences on the activity of the free radicals including: The temperature, pH, light, and presence of metal cations (**Alqahtani, 2014**; **Joshi, 2016**).

When free radicals break one or more double bonds or oxidize the chromphores, the discolored teeth appear bleached and whiter in color this process known as redox reaction (**Machado *et al*., 2016**). The results from these reactions are products, which are low in molecular weight reflect less lights and removed easily from the tooth **(Figure 1.1) (Bonsor and Pearson, 2012)**.

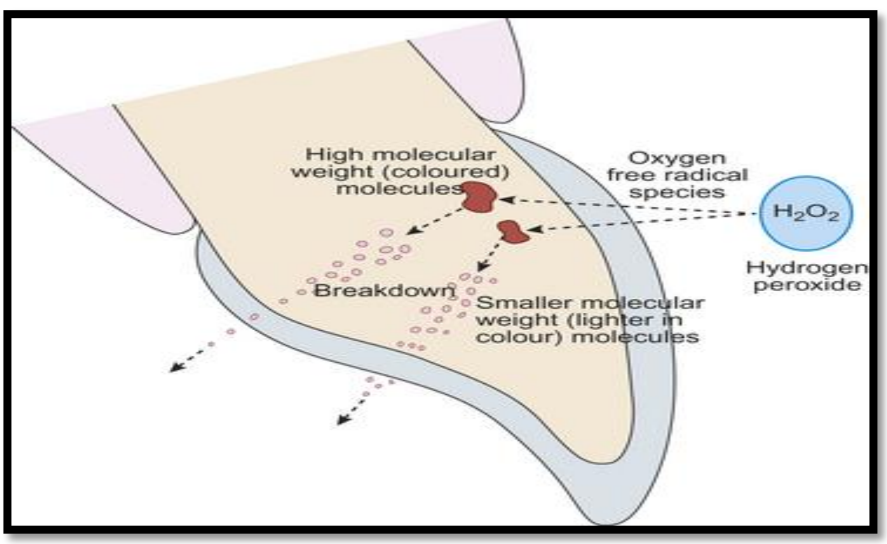

Figure (1.1): Diagram showing the oxygen free radical species entering the tooth, the chemical reaction and the products of the reaction leaving the tooth **(Bonser and Person, 2012).**

3- Surface change and color

The third phase which is the final phase of bleaching process is actually associated with identifying the color change through the changing the tooth surface that became reflects the light differently. Several factors effect on the perception of tooth color, including the type of light, the object, and the viewer. The tooth color is recognized by diffuse reflectance from the dentin through the outer translucent enamel surface. According to color vision, the only light that human eye can observe is the reflected light (**Kwon and Wertz, 2015**).

The dentin is a main factor in determining tooth color moreover it is essential when considering the mechanism of tooth bleaching, in previous study estimated the separate role of enamel and dentin to changing in tooth color during bleaching, and established that the overall change was extremely influenced by the dentin **(Turkun *et al*., 2002).**

It is well recognized that diffuse reflection is more through the rough surface, making the object brighter, while the smooth surface triggers to less reflection. Within the same context, previous studies found that demineralization during tooth bleaching might effect to the whitening efficiency **(Kwon *et al*., 2002; Jiang *et al*., 2008).**This probability was supported by a study suggested that color regression is associated with increasing mineral uptake after tooth whitening **(Li *et al.*, 2010)**.

1.2.2 Composition of commercial bleaching agents:

The bleaching agents comprise both active and inactive ingredients:

1- The active ingredients:

A- Hydrogen peroxide (H2O2): The characteristics of (H2O2) including liquid without color, with a bitter flavor and is extremely soluble in water to give an acidic solution. H2O2 is an oxidizing agent and has several of applications in industry such as in bleaching hair and fur, act as seed disinfectant and use in wine distillation as a neutralizing agent **(Tredwin *et al*., 2006; Goldberg *et al*., 2010)**.

Generally it is somewhat more viscous than water, and has a molar mass of 34.01g/mol. it can penetrate through dentin, due to its low molecular weight which will releases oxygen and thus breakdowns the double bonds of the organic compounds that located inside the dentinal tubules. The concentration of hydrogen peroxide that use in dentistry ranging from 3-40% **(Plotino *et al*., 2008)**.

B- Carbamide peroxide (CH6N2O3): Is really a white transparent solid, when interacts with water it releases oxygen. It used in different whitening products for instance over-the-counter and at- home bleaching. The actual concentrations utilized in bleaching agents ranges from 10-35%. Carbamide peroxide with concentarion 10% solution breakdowns into 3.35% hydrogen peroxide and 6.65%urea **(da Silva Marques *et al.*, 2012)**. Usually Carbamide peroxide products comprise a carbopol base which slow down the release of hydrogen peroxide and remain active for a longer period of time **(De La Pena *et al.*, 2014).**

C- Sodium perborate (NaBO3): Is really a white, water-soluble, odorless and available as a powder. Although it is stable when dry, while in the presence of acid, warm air, or water, it is breakdown to release hydrogen peroxide, sodium metaborate and oxygen (**Kwon and Wertz, 2015).**

D- Chlorine dioxide (ClO2): is a powerful and suitable oxidizing agent. In spite of the safety concerns, previous *in vitro* study revealed that 0.07% of chlorine dioxide whitened teeth in a faster rate than 35% of hydrogen peroxide, however it has many harmful effect on teeth for example teeth turn out to be permanently sensitive and lack of tooth original appeal **(Greenwall, 2008; Ablal *et al.*, 2013).**

2- Inactive ingredient:

A-Thickening agents: The most frequently used thickening agent in bleaching agents is Carbopol (carboxypolymethylene). This agent has two main advantages. First, it makes the bleaching materials more viscose, that makes the bleaching gel retain in the tray for longer period. Second, it increases the active oxygen-releasing time in the bleaching products by around four times (**Rodrigues *et al* 2017, Alqahtani, 2014).**

B-Carrier: The most frequently used carriers in marketable bleaching materials are glycerin and propylene glycol. The carrier can preserve moisture that helps to dissolve other ingredients. The sore throat that occur during bleaching arise from swallowing of glycerin in the solution or gel (**Joiner and Thakker, 2004; joshi, 2016).**

C-Surfactant and pigment dispersants: Bleaching gels is more effective with surfactant or pigment dispersants than those without them. The function of surfactant is permitting the active ingredient in bleaching agent to diffuse (**Gerlach *et al*., 2002; Alqahtani, 2014**).

D- Preservative: Different preservative substances available but sodium benzoate methyl and propylparaben are commonly used. Their function is to prevent bacterial growing in bleaching materials. Furthermore, these agents also have the ability of releasing intermediate metals for example copper, iron and magnesium which accelerate the breakdown of hydrogen peroxide **(Joiner and Thakker, 2004; Joshi, 2016).**

E-Flavoring: Flavorings are ingredients used to enhance the taste and also acceptance of bleaching products by the consumer, for example include peppermint, spearmint, anise, and a sweetener for instance saccharin (**Alqahtani, 2014**).

F- Additives

-Potassium nitrate: It is superior in comparison to other additives. Five percent potassium nitrate acts like an anesthetic by halting the nerve from repolarizing after it has depolarized in the pain cycle. Hence, it decreases the postoperative sensitivity without reducing the bleaching effect. It is effective even in light-activated bleaching **(Raymond and Cook, 2015).**

- Calcium phosphate: Lately, amorphous calcium phosphate (ACP) has been used in the tooth whitening products, in order to reduce sensitivity and add certain shine to teeth **(Ciavoi *et al.*, 2017).**

- Fluoride: Fluoride also demonstrates an additive material to bleaching material. Generally fluoride increases the micro hardness of the enamel. Bleaching gels with fluoride lead to lesser demineralization without changing the bleaching effectiveness. The fluoridated bleaching gels preserve micro tensile, bond strength and support subsequent restorative techniques. Fluoride decreases the sensitivity by blocking the dentinal tubules subsequent slow down the flow of the dentinal fluid **(Joshi, 2016).**

1.2.3 Types of vital tooth bleaching procedures:

There are actually three essential methods regarding to bleaching of the vital teeth including in-office (power bleaching), at-home (dentist supervised night-guard bleaching), and bleaching with over-the-counter (OTC) products **(Goldberg *et al*., 2010).**

1.2.3.1 In-office bleaching

In office bleaching procedure uses a high concentration of H2O2 ranging (25–40%)**.** In this approach, the dentist control during the procedure and when the desired outcome accomplished has the ability to stop the procedure. The peroxide may activate according to the type of bleaching gels either chemically activated or physically activated (heat or light)**(Hegde *et al*., 2012)**

There are different forms of curing lights used to stimulate bleaching gel including Plasma arc lamp, halogen curing lights, Diode lasers (both 830 and 980 nm wavelength diode lasers), or Metal halide (Zoom) light **(Alqahtani, 2014)**. The power bleaching can produce an optimum result in single session but some cases of severe discoloration need more than one session to achieve the perfect result **(Joshi, 2016).**

The advantages of in- office bleaching technique include it is best for patients who do not deal well with bleaching procedure at home, It is favorite for the patient since it is provide fast result from one session and does not need patients compliance, while the main disadvantages of in office bleaching technique is more expensive, more often causes tooth sensitivity and can cause gingival burns (**Reis *et al*., 2018).**

1.2.3.2 Take-home (at home bleaching, Dentist-prescribed home bleaching)

At home bleaching products usually contain carbamide peroxide or hydrogen peroxide. The concentrations used in these product reach up to 21% carbamide peroxide which is equal nearly to 7% hydrogen peroxide and applied for at least 16 days 2 hours a day**.** There are many choices for bleaching teeth at home, the most common include tooth whitening strips and gels, tray-based tooth bleaching systems and tooth whitening toothpastes (**Abouassi *et al*., 2011).**

Dentist-prescribed home bleaching custom-fabricated trays, tacky high-viscosity gels, adequate instructions, and recall exams--has been shown to be an effective method for bleaching teeth. Trays can be worn overnight or during the day with similar effectiveness **(De Geus *et al* 2016).**

1.2.3.3 Over-the-counter (OTC) bleaching

The concentration of whitening agent in these products is ranging (3–6% hydrogen peroxide) which represent a low concentration comparing to other products. It can be applied to the teeth in several ways via strips, gum shields, or paint-on product formats. They are also presented as pre-fabricated trays, toothpastes and whitening dentifrices. It should be applied two times each day for up to 2 weeks (**Zhang *et al*., 2007)**.

1.2.4 Adverse effects of bleaching agents

1.2.4.1 Systemic effects

There is more concern about the possible adverse effects of home-bleaching agents, although their concentrations are far below those of in-office bleaching agents, because the latter are controlled by the dentist. Occasionally, patients report gastrointestinal mucosal irritation, e.g., a burning palate and throat, and minor upsets in the stomach or intestines. However, most reports have concluded that the use of low concentrations of hydrogen peroxide in tooth bleaching is still safe **(Greenwall, 2017)**.

The toxicology of hydrogen peroxide has been revised by the "European Centre for Ecotoxicology and Toxicology of Chemicals"

(Burrows, 2010). Hydrogen peroxide has been establish not to be mutagenic, teratogenic, or carcinogenic **(Greenwall-Cohen and Greenwall, 2017**). However, two previous publications pointed out that hydrogen peroxide used in long-term treatment and at a high concentration might act as a promoter of oral mucosal damage and, moreover, have genotoxic and carcinogenic effects **(Naik *et al*.,2005; Tredwin *et al*.,2006).**

1.2.4.2 Effects of bleaching agents on soft tissues and skin: Some patients may experience gingival or mucosal irritation during home bleaching procedures. Soft tissue irritation may be caused by an ill-fitting tray impinging on the gingiva and/or the use of excess material. Management includes simply adjusting and polishing the tray and or instructing the patient to use less material. During an in-office bleaching procedure, a higher HP (hydrogen peroxide) concentration is usually used. HP is a caustic substance and can cause burns of the gingival or mucosal tissue. Therefore, a rubber dam or light-cured resin, provided by the manufacturer, should always be used to protect soft tissues during in-office bleaching procedures **(Majeed *et al*., 2015).**

Fortunately these burns reported them to be transient and to disappear, either spontaneously or in response to a decrease in the frequency of application, a decrease in the number of hours of usage per day or a cessation of the procedure for a few days and if these burns persist can be treated by application of an antiseptic ointment and rehydration (**Alqahtani, 2014).**

Hydrogen peroxide is not carcinogenic when applied topically to the mouse skin, but they are potent skin irritants. Notable modifications induced by peroxides in skin are epidermal hyperplasia and the induction of dark keratinocytes and H2O2 gave rise to an extensive epidermolysis, inflammation, and vascular injury in rodents. This was found to be followed by a rapid regeneration and epidermal hyperplasia **(Goldberg *et al*., 2010).**

1.2.4.3 Effects of bleaching agents in dental aspect

1- Tooth sensitivity

Tooth sensitivity represents the most commonly side effect of bleaching. Previous studies found that the occurrence of tooth sensitivity during in office or at home bleaching ranging from 18% to 78%. The majority (55%) may experience mild sensitivity whereas 10% experience moderate and only 4% may experience severe sensitivity (**Tredwin *et al.*, 2006; Joshi 2016)**. Clinical trials observed that tooth sensitivity is temporary, and typically persists for about 4 days after the termination of bleaching procedure (**Perchyonok and Grobler, 2015**).

The particular mechanisms of tooth sensitivity after tooth bleaching have not yet been completely recognized. *In vitro* study have revealed that tooth sensitivity largely results from interaction between hydrogen peroxide and the pulp tissue since peroxide can pass through enamel and dentin and reach the pulp chamber (**Reis *et al*., 2013).**

Glycerine, used as a carrier in most bleaching agents, is hydrophilic and causes dehydration of tooth structure during bleaching treatment. This can also result in tooth sensitivity. The use of bleaching products with higher peroxide concentration also increases the risk of tooth sensitivity. Patients that have already a history of tooth sensitivity, they have a higher possibility for such a side effect from tooth bleaching, and this should needs to be taken in concern before undergo bleaching treatment **(Perchyonok and Grobler, 2015).**

Patients with existing sensitivity should be treated before starting bleaching treatment with desensitizing toothpastes and fluoride gels can be used for 2 – 3 weeks prior to the treatment or during treatment. A neutral sodium fluoride gel in a tray can be worn overnight or gels containing 3% to 5% potassium nitrate or fluoride and potassium nitrate in a tray before or after bleaching for 10 - 30 minutes. Furthermore, the frequency and / or duration of application can be reduced and the treatment can also be interrupted, if necessary **(Majeed *et al*., 2015).**

2- Effects of bleaching agent on enamel surface

During tooth bleaching, the pH of bleaching gel causes enamel demineralization since it is known that enamel begins to dissolve if a solution with pH <5.5 was applied on it and this results in surface morphological change and reduction of enamel hardness **(Rodrigues *et al*., 2017)**. In contrast, bleaching gel either with neutral or alkaline pH does not modify the enamel roughness or neither produce harmful effects on the enamel surface **(Nascimento *et al.*, 2014).**

The morphological alteration of the enamel surface increased porosity of the superficial enamel structure, demineralization and decreased protein concentration, organic matrix degradation, modification in the calcium:phosphate ratio, and calcium loss, thereby supporting the hypothesis that bleaching agents are chemically active components potentially able to induce substantial structural alterations in human dental enamel **(Figure 1.2) (Pinto *et al*., 2004; Pedreira De Freitas *et al.*, 2010).** Previous study found that if bleaching remains on enamel more than 60 min may cause significant roughness and decline in micohardness of enamel **(Polydorou *et al*., 2018).**

The bleaching cause different degree of affects according to their methodology, the type of bleaching agent used, the duration of application and load applied. However, human enamel exhibits large regional variations in structure related to the differences in local chemistry (varying levels of mineralization, organic matter and water) and microstructure (fractions of inorganic crystals and organic matrix)**(Braly *et al*., 2007).**

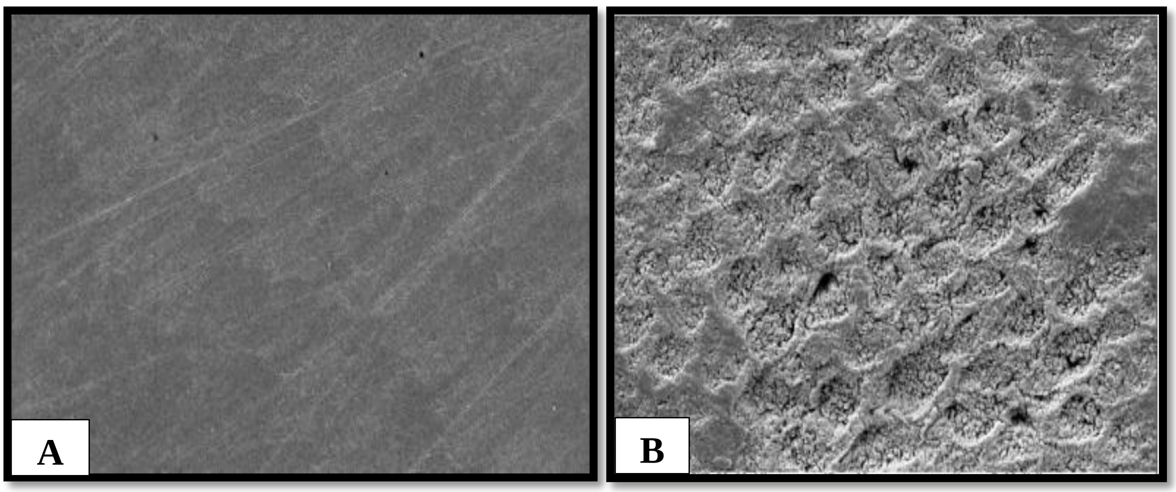

Figure (1.2): Scanning electron microscope of enamel surface **A**: A smooth and unchanged enamel surface morphology of unbleached tooth **B**: Rough enamel surface with mild interprismatic dissolution of bleached tooth (**Pinto *et al*., 2004).**

The bleaching treatments induce changes in surface roughness and consequently influence the formation of supra- and sub-gingival plaque. Therefore, the adhesion of Streptococcus mutants to enamel is increased Such undesirable effect may have some implication on future developments regarding the carious decay **(Hosoya *et al*., 2003).**

It should be considered that enamel demineralization is an undesirable effect resulting from bleaching agents, related to their concentration and to the time necessary to obtain teeth whitening. Remineralization due to saliva may restore gradually the mineral charge of enamel surfaces, but the specific organic matrix is definitively degraded, and this alteration may interfere with enamel repair. Attempts to reduce the loss of mineral and the formation of microdefects on enamel surface were carried out with fluoride containing bleaching agents shown to induce less enamel surface demineralization and altered microhardness **(Chen *et al*., 2008).**

3- Effects of bleaching agent on dentin

The mechanical properties of dentin are of significant interest because dentin provides the bases for both enamel and cementum. Moreover, dentin is largely responsible for the structural integrity of the entire tooth. Slight changes in surface morphology and hardness have been identified in dentin after bleaching **(de Freitas *et al*., 2002).** It have been hypothesized that HP and CP cause changes to the organic component of dentin by a mechanism of dentin denaturation or protein oxidation. Protein degradation has been reported after treatment with HP or other antioxidants. Urea is an important component of CP and is commonly used in the laboratory as a protein-denaturing agent **(Berger *et al.*, 2014).**

According to **Maleknejad *et al*. (2012)** the scanning electron microscope (SEM) results showed that the bleaching with all whitening agents caused a significant increase in tubule diameter**(Figure 1.3)**. The greatest changes in tubule's diameters has been found in 45% Carbamide peroxide group in spite of the fact that its hydrogen peroxide concentration was lower than 35% hydrogen peroxide and also it showed a significant reduction in calcium content. This increase in dentinal tubule diameter might be caused by mineral loss and widening of tubule orifices as a result of oxidation of proteins (**Martin-Biedman *et al*., 2010).**

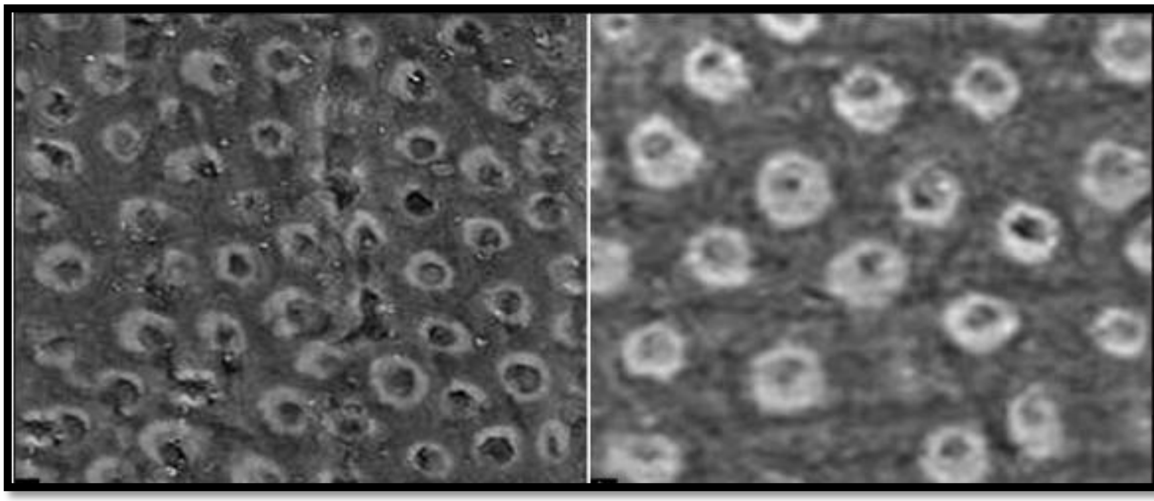

Figure (1.3): Scanning electron microscope of dentin surface shows increased dentinal tubule diameter after bleaching procedure (**Maleknejad *et al*., 2012).**

In a study conducted by **Basting *et al*. (2003),** results showed that the thickening agent (carbopol and/or glycerin), not just the 10% carbamide peroxide, caused a decrease in dentin microhardness. In addition, **Faraoni-Romano *et al*. (2008)** studied the effects of low and highly concentrated bleaching agents on microhardness and surface roughness of bovine enamel and dentin and proved that while bleaching did not change enamel microhardness and surface roughness, it affected dentin in terms of microhardness, which seems to be dependent on the bleaching agent used.

It has been demonstrated that the penetration of bleaching agent through the mineralized tissues of bovine teeth, increasing the dental permeability. However, some factors such as the enamel thickness, existence of enamel fractures and cracks, permeability, and direction of the dentinal tubules, influence the diffusion of bleaching agents through dentin **(Berger *et al*., 2013).**

Peroxide treatment may alter the chemical structure of dentin, reduce the potassium levels and affect the calcium-potassium ratio. Thus, some manufactures of bleaching agents have added calcium and fluoride to the agents. This approach reduces mineral loss during bleaching treatment, with little influence on the organic components of dental tissues **(Giannini *et al.*, 2006).**

4- Effect of bleaching agent on dental pulp

Hydrogen peroxide must diffuse through the enamel to reach the underlying dentin, which is typically responsible for tooth color in order to bleach the teeth. However, *in vitro* study has confirmed that because of the low molecular weight of H2O2 even at low concentrations can diffuse through dentine via the dentinal tubules and influence the pulp chamber (**de Almeida *et al*., 2015**).

The penetration of H2O2 and its adverse effects on pulp can be enhance by a number of factors including higher concentration of peroxide **(Vas *et al*., 2016)**, longer time of application results in releasing more ROS in the pulp **(De Geus *et al*., 2016),** increased temperature (**Mollica *et al*., 2010)**. The acidic pH could cause enamel surface demineralization and increase in the porosities of the enamel accordingly, greater and faster penetration of H2O2 into the pulp chamber **(Balladares *et al.*, 2019)**, larger size of dentinal tubules **(Llena *et al*., 2018)**, light activation as results in increase the temperature of the tooth (**Gonçalves *et al*., 2016**), as well as the presence of restoratration as microleakage from restorations margins can be reflected a probable way for H2O2 penetration into the pulp chamber **(Camargo *et al*., 2007).**

Hydrogen peroxide acts as an oxidizing agent by producing free radicals including reactive oxygen molecules and hydrogen peroxide anions which are either produced by the organism like mitochondria as a normal cell metabolic activity or developed by exogenous sources like bleaching agent. Low levels of ROS serve in many different regulatory functions including (increased growth activity, cell proliferation, tissue repair, and angiogenesis) **(Buchalla and Attin, 2007; Jha *et al*., 2017).**

Reactive oxygen radicals have the ability to diffuse through different mechanical barrier of the teeth as have the ability to penetrate through interprismatic spaces and dentinal tubules and overwhelmed numerous defense mechanisms, including the odontoblastic process, dentinal fluids, and collagen fibers consequently reach the pulp **(Soares *et al*., 2011)**.

As the free radicals contact with the pulp tissue different defense systems have developed to overcome the accumulation of ROS. These include numerous non-enzymatic molecules including vitamins A, E, C, glutathione, and flavonoids, as well as antioxidant enzyme including superoxide dismutases (SOD), glutathione peroxide and catalase **(Martindale and Holbrook, 2002)**. Probably higher level of ROS will result in oxidative stress to the pulp cells because of the unbalance between the production of reactive oxygen species (ROS) and the pulpal enzymes that protect the pulp from H2O2 degradation which are significantly inhibited by the action of hydrogen peroxide in bleaching agent and this results in pulpal damage ranging from a temporary inflammatory reaction to the incidence of local necrosis **(Patri *et al*., 2013)**.

Concerning animal studies **Hadi and AL-Ghaban (2020)** showed that the diffusion of products of a 40 % of H2O2 bleaching gel degradation caused necrosis and inflammatory reaction in molars pulp of rat **(Figure 1.4 A,B).**

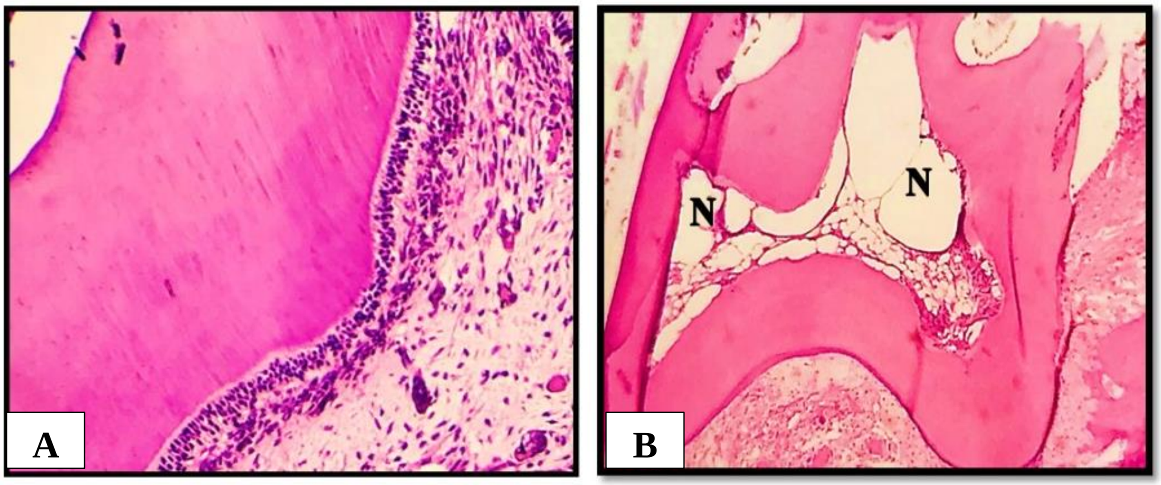

Figure (1.4): A: Histological view of unbleached molar tooth shows normal pulp tissue **B:** Histological view of bleached molar shows diffuse necrotic areas (N) in pulp chamber **(Hadi and AL-Ghaban, 2020).**

Regarding human studies **de Souza Costa *et al*. (2010)** reported areas of necrosis in human lower incisors after bleaching treatment, while **Kina *et al*. (2010**) found that there were no pulp changes in human premolars treated with in office bleaching. This controversy in the pulp response regarding different studies because there are several factors contributing for penetration the H2O2 products therefore causing different degrees of adverse effects and responses **(Kwon and Wertz, 2015).**

1.2.4.4 Effect of bleaching agent on restorative materials

hydrogen peroxide (HP) and carbamide peroxide (CP), the most popular bleaching products, can change the physical properties of dental restorations such as their colour, surface roughness, hardness and ion leakage **(El-Murr *et al*., 2011).**

1-Amalgam

A number of studies have found that CP and HP change the properties of dental amalgam restorations, such as ion leakage, microhardness and surface roughness. Previous study found a significant increase in the release of metal ions from dental amalgams exposed to different concentration of HP **(Al-Salehi *et al*., 2007).** Because the release of mercury, silver, copper and tin from the dental amalgams did not exceed the limits defined by the World Health Organization, it concluded that bleaching teeth with amalgam restorations is not a health hazard. Another study identified some factors involved in the bleaching treatment, such as the age of the dental amalgam, an unpolished amalgam surface and the acidity of the bleaching agent, as possible causes of increased release of mercury **(Ahn *et al*., 2006).**

Previous case report revealed amalgam staining of the bleaching tray was detected in correspondence of the left and right first upper molars following tooth whitening for a week. the authors supported that this phenomena was related either to surface oxidation following the bleaching gel exposure or the amalgam superficial chipping may be responsible for the finding **(Figure 1.5)(Deliperi, 2007).**

Figure (1.5): Amalgam staining of the bleaching tray **(Deliperi, 2007).**

Concerned about the surface roughness and the microhardness of dental amalgams after bleaching procedures, some authors studied the impact of bleaching agents on these 2 properties and found no significant changes **(Ahn *et al*., 2006; Al-Salehi *et al*., 2007).**

Coating of amalgam restorations with a protective varnish such as Copalite before bleaching procedure has been reported to reduce release of mercury into the surrounding environment. The corrosion potential of amalgam is also decreased if restorations are polished prior to the bleaching therapy, However, clinicians should monitor defective amalgam restorations during the tooth whitening therapy. Alternatively, their replacement should be considered prior to bleaching **(Deliperi, 2007).**

2-Porcelain

A number of articles have studied the impact of bleaching treatment on the physical properties of ceramic restorations. In previous vitro study revealed that porcelain had a rougher surface after 21 days of exposure to 10% and 35% CP. According to the authors, the changes over the porcelain's surface may have been caused by a reduction of silicon dioxide (SiO_2) and potassium peroxide (K_2O_2) molecules **(Moraes *et al*., 2005).**

Because the increased ceramic roughness could lead to more plaque retention, bacterial adherence and gingival irritation, the authors suggested protecting these materials with a barrier before bleaching to preserve the integrity of the ceramic surface. Laboratory studies of in-office (38% HP) and at-home (15% CP) bleaching agents concluded that the microhardness of ceramic restorations was not affected 30 days after the end of the bleaching procedure **(Polydorou *et al*., 2007).**

While other study found a significant decrease of 15% in the surface microhardness of porcelain 30 days after bleaching with 10% and 16% CP. Overall, these studies show that bleaching could affect the microhardness and surface roughness of porcelain **(Turker and Biskin, 2002).**

3-Glass Ionomer Cement and Resin-Modified Glass Ionomer Cement

Several studies have evaluated the effects of bleaching agents on glass ionomer and resin modified glass ionomer cements. A previous study found a significant difference in the colour of a conventional glass ionomer cement restoration after 4 weeks of bleaching. Additionally SEM revealed a slight surface dissolution **(Li and Yu, 2009)**.

Similarly, another study found alterations, such as cracks and pits, in the surface of the glass ionomer cement, which were explained by the ability of the bleaching agent to alter the surface properties of the material. The authors also found that bleached glass ionomer restorations were more susceptible to different staining solutions such as red wine, herbal tea, Coca Cola and coffee **(Figure 1.6)(Yu *et al*., 2009).**

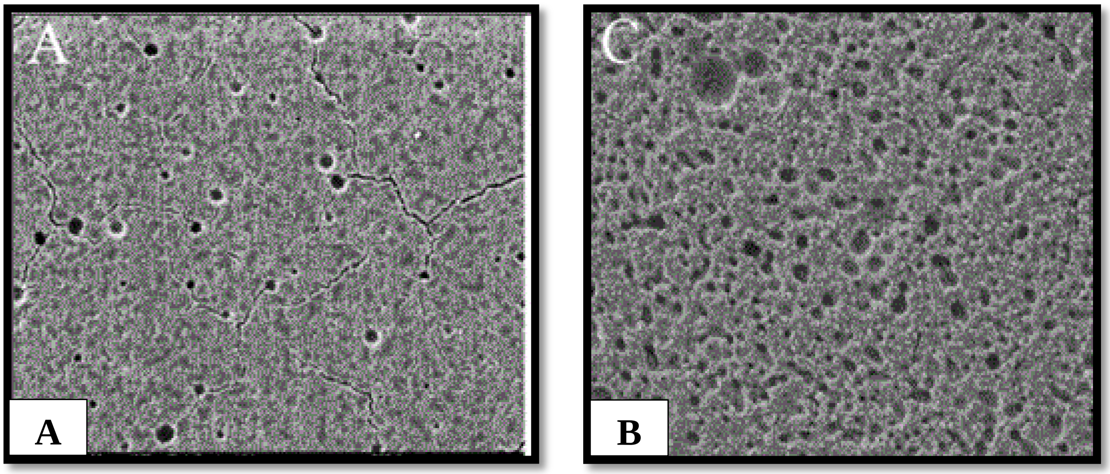

Figure (1.6): Environmental scanning electron microscope observation of the glass-ionomer cement specimens **A:** unbleached specimen shows few cracking areas **B:** bleached specimen shows more cracks and pits on the surface **(Yu *et al*., 2009).**

Other study found a softening effect and a significant decrease in their surface hardness. The author attributed these results to multiple air bubbles mixed into the material that can affect the final properties of the restorations. Consequently, because glass ionomer and resin modified glass ionomer cement restorations are changed when bleached, they may need to be replaced **(Taher *et al*., 2005).**

4-Composite Resins

Many studies have examined the changes that bleaching causes in the characteristics of composite resins, a material commonly used for esthetic dental treatments, such as colour, surface hardness and roughness, staining susceptibility and microleakage. Previous study found significant changes in the color of nanohybrid and packable composite resins after bleaching with 15% CP **(Li and Yu, 2009).** Another study found that this difference was especially noticeable when a high peroxide concentration (35% HP) was used on low-density resins such as microfilled composite resin. In both studies, the color change was clinically acceptable **(Hubbezoglu *et al.*, 2008).**

Hannig *et al.(*2006) reported a significant decrease in the surface hardness of bleached composite resins, not only on superficial surfaces, but in the deeper layers of the filling materials as well. Similarly, another research study concluded that bleaching with different peroxide concentrations significantly decreased the surface microhardness of a microfilled composite resin. These results were related to the high oxidation and degradation of the resinous matrix in the composites (**Taher *et al*., 2005).**

Yu *et al*. (2009) found that bleached composite resins stain more easily than unbleached ones. The authors suggested that this staining could be caused by alterations in the surface of the bleached restorations. Unlike enamel, composite restorations do not change color when bleached. Therefore, they may not require replacing to match the color of bleached enamel after teeth whitening **(Villalta *et al.*, 2006).**

1.2.4.5 Effects of bleaching agent on enamel ⁄ dentine bonding

Bleaching may effects on Bonding to enamel ⁄ dentine, most of the studies showed that when bonding procedure was achieved directly after completion of bleaching treatment, both tensile strength and shear strength of composite resin bonds to enamel considerably reduced **(Topcu *et al*., 2017).**

Bleaching can also adversely effects on bonding between glass ionomer and dentine and this because of precipitations of hydrogen peroxide on the cut surface of dentin **(Muraguchi *et al*., 2007).** It have been suggested to solve these clinical problems related to bleaching procedures, delaying bonding and waiting up to 10 days after bleaching procedure **(Oz and Kutuk, 2018).**

Conclusion

The increasing demand for a better appearance and whiter smile, has made vital tooth-bleaching (also referred to as tooth-whitening) a popular dental procedure. It has developed into one of the fastest growing areas of aesthetic dentistry. It provides a more conservative treatment approach for discolored teeth as compared to other restorative treatment modalities such as composite fillings, veneers or crowns. However, many adverse effects of vital tooth bleaching were revealed on tooth structures, soft tissue and restorations.

Altogether, all these effects have to be taken into consideration prior to deciding if a whitening treatment is necessary or, for that matter, safe. In many cases, it seems rather an artificial cosmetic fashion requirement than a deserving cause. Finally, the control of bleaching effects should stand in the hand of dental surgeons (or at least be under their control), and entists should educate themselves to be able to inform their patients about the benefits and risks of different whitening methods based on the current scientific evidence and to suggest the best treatment option based on a correct diagnosis.

References

(A)

- Ablal, M.A., Adeyemi, A.A. and Jarad, F.D. (2013) The whitening effect of chlorine dioxide: An in vitro study. *Journal of Dentistry*, 41, 76-81.
- Abouassi, T., Wolkewitz, M. and Hahn, P. (2011) Effect of carbamide peroxide and hydrogen peroxide on enamel surface: An in vitro study. *Clinical Oral Investigations*, 15(5), 673-680.
- Ahn HJ, Song YB, Lee YE, Lee JT, Cho SA, Kim KH.(2006) Surface change of dental amalgam after treatment with 10% carbamide peroxide. Dent Mater ,25(2):303-8.
- Alqahtani, M.Q. (2014) Tooth-bleaching procedures and their controversial effects: A literature review. *The Saudi Dental Journal*, 26(2), 33-46.
- Al-Salehi SK, Hatton PV, McLeod CW, Cox AG.(2007) The effect of hydrogen peroxide concentration on metal ion release from dental amalgam. J Dent,35(2):172-6. Epub 2006 Sep 1.

(B)

- Balladares, L., Alegría-Acevedo, L.F., Montenegro-Arana, A., Arana-Gordillo, L.A., Pulido, C., Salazar-Gracez, M.T., Reis, A. and Loguercio, A.D. (2019) Effects of pH and Application Technique of In-office Bleaching Gels on Hydrogen Peroxide Penetration into the Pulp Chamber. *Operative dentistry*, *44*(6), pp.659-667.

- Basting, R.T., Rodrigues Jr., A.L., Serra, M.C.(2003)The effects of seven carbamide peroxide bleaching agents on enamel microhard-ness over time. J. Am. Dent. Assoc. 134, 1335–1342.
- Berger, S.B., Pazenhagen, R., Martinelli, N., Moura, S.K., Carvalho, R.V. and Guiraldo, R.D. (2014) Effect of bleaching agents on the flexural strength of bovine dentin. *J Contemp Dent Pract*, *15*, pp.24-27.
- Berger, S.B., Tabchoury, C.P., Ambrosano, G.M. and Giannini, M. (2013) Hydrogen peroxide penetration into the pulp chamber and dental permeability after bleaching. *General dentistry*, *61*(3), p.e21.
- Bonsor, S. J. and Pearson, G. (2012) *A clinical guide to applied dental materials*, Elsevier Health Sciences.
- Braly A, Darnell LA, Mann AB, Teaford MF, Weihs TP.(2007)
- Buchalla, W. and Attin, T. (2007) External bleaching therapy with activation by heat, light or laser- a systematic review. *Dental materials*, *23*(5), pp.586-596.
- Burrows, S. (2010) A review of the safety of tooth bleaching. *South African Dental Journal*, 65(1), 6-13.

(C)

- Camargo, S.E.A., Valera, M.C., Camargo, C.H.R., Mancini, M.N.G. and Menezes, M.M. (2007) Penetration of 38% hydrogen peroxide into the pulp chamber in bovine and human teeth submitted to office bleach technique. *Journal of Endodontics*, *33*(9), pp.1074-1077.
- Clifton M. (2014) "Tooth Whitening: What We Now Know". The Journal of Evidence-Based Dental Practice. 14 Suppl: 70–76. doi:10.1016/j.jebdp.2014.02.006.

- Carey, C. M. (2014) Tooth whitening: what we now know. *Journal of Evidence Based Dental Practice*, 14, 70-76.
- Casado, B. G., Moraes, S. L., Souza, G. F., Guerra, C. M., Souto-Maior, J. R., Lemos, C. A., Vasconcelos, B. C. and Pellizzer, E. P. (2018) Efficacy of dental bleaching with whitening dentifrices: A systematic review. *International Journal of Dentistry*.
- Chen, H.P., Chang, C.H., Liu, J.K., Chuang, S.F. and Yang, J.Y., 2008. Effect of fluoride containing bleaching agents on enamel surface properties. Journal of dentistry, 36(9), pp.718-725.
- Ciavoi, G., Bechir, A., Suciu, M., Bechir, E. S., Doda, L., Olteanu, C. and Dascalu, I. T. (2017) The Role of Peroxide Based Bleaching Agents in the Induction of Tooth Sensitivity. *Revista De Chimie*, 68(5), 911-915.

(D)

- da Silva Marques, D. N., Lourenco Silveira, J. M., Oliveira Faria Marques, J. R., Almeida Amaral, J., Marques Guilherme, N., Da Mata, P. and Sola, A. D. (2012) Kinetic release of hydrogen peroxide from different whitening products. *European Journal of Esthetic Dentistry*, 7(3).
- de Almeida, L. C. A. G., Soares, D. G., Gallinari, M. O., De Souza Costa, C. A., Dos Santos, P. H. & Briso, A. L. F. (2015) Color alteration, hydrogen peroxide diffusion, and cytotoxicity caused by in-office bleaching protocols. *Clinical Oral Investigations*, 19(3), 673-680.
- de Freitas PM, Basting RT, Rodrigues AL, Serra MC.(2002) Effects of two 10% peroxide carbamide bleaching agents on dentin microhardness at different time intervals. Quintessence International ,33(5):370-375.

- De Geus, J., Wambier, L., Kossatz, S., Loguercio, A. and Reis, A. (2016) At-home vs in-office bleaching: a systematic review and meta-analysis. *Operative Dentistry*, 41(4), 341-356.
- De La Pena, V. A. & Ratón, M. L. (2014) Randomized clinical trial on the efficacy and safety of four professional at-home tooth whitening gels. *Operative Dentistry*, 39(2), 136-143.
- de Souza Costa, C. A., Riehl, H., Kina, J. F., Sacono, N. T. and Hebling, J. (2010) Human pulp responses to in-office tooth bleaching. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, 109(4), 59-64.
- Deliperi, S.(2007) Interaction of peroxides with amalgam: a case report. *Journal of Esthetic and Restorative Dentistry*, *19*(4), pp.208-211.

(E)

- El-Murr, J., Ruel, D. and St-Georges, A.J.(2011) Effects of external bleaching on restorative materials: a review. *J Can Dent Assoc*, *77*(b59), pp.1-6.

(F)

- Faraoni-Romano, J.J., Da Silveira, A.G., Turssi, C.P., Serra, M.C.(2008) Bleaching agents with varying concentrations of carbamide and/or hydrogen peroxides: effect on dental microhardness and roughness. J. Esthet. Restor. Dent. 20, 395–402, discussion 403-394.

(G)

- Gerlach, R., Zhou, X. and Mcclanahan, S. (2002) Comparative response of whitening strips to a low peroxide and potassium nitrate bleaching gel. *American Journal of Dentistry*, 15, 1.

- Giannini M, Silva AP, Cavalli V, Leme AF.(2006) Effect of carbamide peroxide-based bleaching agents containing fluoride or calcium on tensile strength of human enamel. J Appl Oral Sci ,14(2):82-87.
- Goldberg, M., Grootveld, M. and Lynch, E. (2010) Undesirable and adverse effects of tooth-whitening products: a review. *Clinical oral investigations*, 14(1), 1-10.
- Goncalves, R., Costa, C., Soares, D., Santos, P. D., Cintra, L. and Briso, A. (2016) Effect of different light sources and enamel preconditioning on color change, H2O2 penetration, and cytotoxicity in bleached teeth. *Operative dentistry*, 41(1), 83-92.
- Greenwall, L. 2017. Tooth Whitening Materials. *Tooth Whitening Techniques*, 2^{nd} ed, CRC press, US, 37-63.
- Greenwall, L. H. (2008) The dangers of chlorine dioxide bleaching. *Aesthetic Dentistry Today*, 2, 20–22.
- Greenwall-Cohen, J. and Greenwall, L. (2017) Carbamide peroxide and its use in oral hygiene and health. *Dental Update*, 44(9), 863-869.

(H)

- Hadi, R.J. and AL-Ghaban, N.M.(2020) Histological evaluation of pulp response to in-office bleaching technique in rats. *Biochem. Cell. Arch*. 20(2), pp. 6095-6100.
- Hannig C, Duong S, Becker K, Brunner E, Kahler E, Attin T.(2006) Effect of bleaching on subsurface microhardness of composite and a polyacid modified composite. Dent Mater.;23(2):198- 203.
- Hegde M, Shetty K, Shetty S.(2012) Overview of in-office bleaching of vital teeth. IRJP ,3:12-6.

- Hosoya, N., Honda, K., Iino, F. and Arai, T., 2003. Changes in enamel surface roughness and adhesion of Streptococcus mutans to enamel after vital bleaching. Journal of dentistry, 31(8), pp.543-548.
- Hubbezoglu I, Akaoglu B, Dogan A, Keskin S, Bolayir G, zçelik S, et al.(2008) Effect of bleaching on color change and refractive index of dental composite resins. Dent Mater J,27(1):105-16

(J)

- Jha, N., Ryu, J.J., Choi, E.H. and Kaushik, N.K. (2017) Generation and role of reactive oxygen and nitrogen species induced by plasma, lasers, chemical agents, and other systems in dentistry. *Oxidative medicine and cellular longevity*.
- Jiang, T., Ma, X., Wang, Y., Tong, H., Shen, X., Hu, Y. and Hu, J. (2008.) Investigation of the effects of 30% hydrogen peroxide on human tooth enamel by Raman scattering and laser-induced fluorescence. *Journal of Biomedical Optics*, 13(1).
- Joiner, A. and Thakker, G. (2004) In vitro evaluation of a novel 6% hydrogen peroxide tooth whitening product. *Journal of Dentistry*, 32, 19-25.
- Joshi, S. B. (2016) An overview of vital teeth bleaching. Journal of Interdisciplinary Dentistry, 6(1), 3.

(K)

- Kapadia, Y. and Jain, V. (2018) Tooth staining: A review of etiology and treatment modalities. *Acta Scientific Dental Sciences*, 2(6), 67-70.
- Karaarslan ES, Özmen ZC, Aytac F, Bicakci AA, Buldur M, et al. (2019) Evaluation of biochemical changes in dental tissues after different office

bleaching methods. Human and Experimental Toxicology 38(4): 389-397.

- Kanokrungsee, T. and Leevailoj, C. (2014) Porcelain veneers in severely tetracycline-stained teeth: A clinical report. Mahidol Dental Journal, 34(1), 55-69.
- Kihn, P. W. (2007) Vital tooth whitening. *Dental Clinics of North America*, 51(2), 319-331.
- Kina, J., Huck, C., Riehl, H., Martinez, T., Sacono, N., Ribeiro, A. and Costa, C. A. D. S. (2010) Response of human pulps after professionally applied vital tooth bleaching. *International Endodontic Journal*, 43(7), 572-580.
- Kwon, S. R. and Wertz, P. W. (2015) Review of the mechanism of tooth whitening. *Journal of Esthetic and Restorative Dentistry*, 27(5), 240-257.
- Kwon, Y., Huo, M., Kim, K., Kim, S. and Kim, Y. (2002) Effects of hydrogen peroxide on the light reflectance and morphology of bovine enamel. *Journal of Oral Rehabilitation*, 29(5), 473-477.

(L)

- Li Q, Yu H, Wang Y.(2009) Colour and surface analysis of carbamide peroxide bleaching effects on the dental restorative materials in situ. J Dent,37(5):348-56. Epub 2009 Feb 8.
- Li, Q., Xu, B., Li, R., Yu, H. and Wang, Y. (2010) Quantitative evaluation of colour regression and mineral content change of bleached teeth. *Journal of Dentistry*, 38(3), 253-260.
- Llena, C., Martínez-Galdón, O., Forner, L., Gimeno-Mallench, L., Rodríguez-Lozano, F. J. and Gambini, J. (2018) Hydrogen Peroxide Diffusion through Enamel and Dentin. *Materials*, 11(9), 1694.

(M)

- Machado, L. S., Anchieta, R. B., Dos Santos, P. H., Briso, A., Tovar, N., Janal, M. N., Coelho, P. G. and Sundfeld, R. H. (2016) Clinical comparison of at-home and in-office dental bleaching procedures: a randomized trial of a split-mouth design. The International Journal of Periodontics and Restorative Dentistry, 36(2), 251-60.
- Majeed, A., Farooq, I., Grobler, S. R. and Rossouw, R. (2015) Tooth-bleaching: a review of the efficacy and adverse effects of various tooth whitening products. Journal of the College of Physicians and Surgeons Pakistan, 25(12), 891-6.
- Maleknejad, F., Ameri, H. and Kianfar, I. (2012) Effect of intracoronal bleaching agents on ultrastructure and mineral content of dentin. *Journal of conservative dentistry: JCD*, *15*(2), p.174.
- Martin-Biedman B, Gonzalez-Gonzalez T, Lopes M, Lopes L, Vilar R, Babillo J, et al.(2010) Colorimeter and scanning electron microscopy analysis of teeth submitted to internal bleaching. *J Endod*,36:334–7.
- Martindale, J.L. and Holbrook, N.J. (2002) Cellular response to oxidative stress: signaling for suicide and survival. *Journal of cellular physiology*, *192*(1), pp.1-15.
- Mollica, F. B., Rocha, D. M. D., Travassos, A. C., Valera, M. C. and Araujo, M. A. (2010) Temperature variation in pulp chamber during dental bleaching in presence or absence of light activation. *Journal of Dental Science*, 25(4), 382-385.
- Moraes RR, Marimon JL, Schneider LF, Correr Sobrinho L, Camacho GB, Bueno M.(2005)Carbamide peroxide bleaching agents: effects on

surface roughness of enamel, composite and porcelain. Clin Oral Investig. 2006;10(1):23-8.

- Mortazavi, H., Baharvand, M. and Khodadoustan, A. (2014) Colors in tooth discoloration: a new classification and literature review. *International Journal of Clinical Dentistry*, 7(1).
- Muraguchi, K., Shigenobu, S., Suzuki, S. and Tanaka, T. (2007) Improvement of bonding to bleached bovine tooth surfaces by ascorbic acid treatment. *Dental Materials Journal*, 26(6), 875-881.

(N)

- Nadhum, N. S. and Al-Khafaji, A. H. (2014) The effect of in office bleaching on surface roughness and micro-hardness of newly developed composite materials: In Vitro Study. *Journal of Baghdad College of Dentistry*, 325(2214), 1-6.
- Naik S, Tredwin CJ, Scully C (2005) Hydrogen peroxide toothwhitening
- Nascimento, W.C., Gomes Ydo, S., Alexandrino, L.D., Costi, H.T., Silva Jr, J.O. and Silva, C.M. (2014) Influence of fluoride concentration and pH Value of 35% hydrogen peroxide on the hardness, roughness and morphology of bovine enamel. *J Contemp Dent Pract*, *15*(4), pp.392-8.

(O)

- Oz, F.D. and Kutuk, Z.B.(2018) Effect of various bleaching treatments on shear bond strength of different universal adhesives and application modes. *Restorative Dentistry & Endodontics*, *43*(2).

(P)

- Patri, G., Agnihotri, Y., Rao, S. R., Lakshmi, N. and Das, S. (2013) An in vitro spectrophotometric analysis of the penetration of bleaching agent into the pulp chamber of intact and restored teeth. *Journal of Clinical and Diagnostic Research*, 7(12), 3057.

- Patri, G., Agnihotri, Y., Rao, S. R., Lakshmi, N. and Das, S. (2013) An in vitro spectrophotometric analysis of the penetration of bleaching agent into the pulp chamber of intact and restored teeth. *Journal of Clinical and Diagnostic Research*, 7(12), 3057.
- Pedreira De Freitas AC, Espejo LC, Botta SB, De Sa Teixeira, Cerqueira Luz A, Narciso GN.(2010) AFM analysis of bleaching effects on dental enamel microtopography. Appl Surf Sci ,256:2915-9. ￼
- Perchyonok, V. and Grobler, S. (2015) Tooth-bleaching: mechanism, biological aspects and antioxidants. *International Journal of Dentistry and Oral Health*, 1(3), 1-7.
- Pini, N.I.P., Sundfeld-Neto, D., Aguiar, F.H.B., Sundfeld, R.H., Martins, L.R.M., Lovadino, J.R. and Lima, D.A., (2015) Enamel microabrasion: An overview of clinical and scientific considerations. *World Journal of Clinical Cases*, *3*(1), p.34
- Pinto, C. F., Oliveira, R. D., Cavalli, V. and Giannini, M. (2004) Peroxide bleaching agent effects on enamel surface microhardness, roughness and morphology. *Brazilian Oral Research*, 18(4), 306-311
- Plotino, G., Buono, L., Grande, N. M., Pameijer, C. H. & Somma, F. (2008) Nonvital tooth bleaching: a review of the literature and clinical procedures. *Journal of Endodontics*, 34(4), 394-407.
- Polydorou O, M◌nting JS, Hellwig E, M.(2007)Auschill TM. Effect of in-office tooth bleaching on the microhardness of six dental esthetic restorative materials. Dent Mater,23(2):153-8. Epub 2006 Feb 10.

- Polydorou, O., Scheitza, S., Spraul, M., Vach, K. And Hellwig, E., (2018) The effect of long-term use of tooth bleaching products on the human enamel surface. *Odontology*, 106(1), 64-72
- Pontes, M.M.A., Gomes, J.M.L., Lemos, C.A.A., Leão, R.S., Moraes, S.L.D., Vasconcelos, B.C.E. and Pellizzer, E.P.(2020) Effect of Bleaching Gel Concentration on Tooth Color and Sensitivity: A Systematic Review and Meta-analysis. *Operative Dentistry*, *45*(3), pp.265-275.
- Prathap, S., Rajesh, H., Boloor, V. A. and Rao, A. S. (2013) Extrinsic stains and management: A new insight. *Journal of Academic Industry Research*, 1(8), 435.

(R)

- Raymond J, Cook D. (2015) Still leaving stains on teeth-the legacy of minocycline? Australas Med J.
- Reis, A., Da Silva, L. M., Martins, L. and Loguercio, A. (2018) In-office tooth whitening. *Clinical Dentistry Reviewed*, 2, 10.
- Reis, A., Kossatz, S., Martins, G. and Loguercio, A. (2013) Efficacy of and effect on tooth sensitivity of in-office bleaching gel concentrations: a randomized clinical trial. *Operative Dentistry*, 38(4), 386-393.
- Rodrigues, F., Serro, A., Polido, M., Ramalho, A. and Figueiredo-Pina, C. (2017) Effect of bleaching teeth with hydrogen peroxide on the morphology, hydrophilicity, and mechanical and tribological properties of the enamel. *Wear*, 374, 21-28.

(S)

- Soares, D.G.S., Ribeiro, A.P.D., Sacono, N.T., Coldebella, C.R., Hebling, J. and De Souza Costa, C.A. (2011) Transenamel and transdentinal cytotoxicity of carbamide peroxide bleaching gels on odontoblast-like MDPC-23 cells. *International endodontic journal*, *44*(2), pp.116-125.

- Sulieman, M. (2005) An overview of tooth discoloration: extrinsic, intrinsic and internalized stains. *Dental Update*, 32(8), 463-471.

(T)

- Taher NM.(2005)The effect of bleaching agents on the surface hardness of tooth colored restorative materials. J Contemp Dent Pract,6(2):18-26.
- The Glossary of Prosthodontic Terms (2017) Ninth Edition, *Journal of Prosthetic Dentistry,* 1-105.
- Topcu, F. T., Erdemir, U., Ozel, E., Tiryaki, M., Oktay, E. A. and Yildiz, E. (2017) Influence of bleaching regimen and time elapsed on microtensile bond strength of resin composite to enamel. *Contemporary Clinical Dentistry*, 8(3), 451.
- Tredwin, C., Naik, S., Lewis, N. and Scully, C. (2006) Hydrogen peroxide tooth-whitening (bleaching) products: review of adverse effects and safety issues. *British Dental Journal*, 200(7), 371-376.
- Turker SB, Biskin T.(2002) The effect of bleaching agents on the microhardness of dental aesthetic restorative materials. J Oral Rehabil,29(7):657-61.
- Türkün, M., Sevgican, F., Pehlivan, Y. and Aktener, B. O. (2002) Effects of 10% carbamide peroxide on the enamel surface morphology: a scanning electron microscopy study. *Journal of Esthetic and Restorative Dentistry*, 14(4), 238-244.

(V)

- Vaz, M. M., Lopes, L. G., Cardoso, P. C., Souza, J. B. D., Batista, A. C., Costa, N. L., Torres, É. M. and Estrela, C. (2016) Inflammatory response of human dental pulp to at-home and in-office tooth bleaching. *Journal of Applied Oral Science*, 24(5), 509-517.
- Villalta P, Lu H, Okte Z, Garcia-Godoy F, Powers JM.(2006) Effects of staining and bleaching on color change of dental composite resins. J Prosthet Dent.95(2):137-42.

(X)

- Xu, B., Li, Q. and Wang, Y. (2011) Effects of pH values of hydrogen peroxide bleaching agents on enamel surface properties. *Operative dentistry*, *36*(5), pp.554-562.

(Y)

- Yu H, Pan X, Lin Y, Li Q, Hussain M, Wang Y.(2009) Effects of carbamide peroxide on the staining susceptibility of tooth-colored restorative materials. Oper Dent,34(1):72-82.

(Z)

- Zhang, C., Wang, X., Kinoshita, J.-I., Zhao, B., Toko, T., Kimura, Y. and Matsumoto, K. (2007) Effects of KTP laser irradiation, diode laser, and LED on tooth bleaching: a comparative study. *Photomedicine and Laser Surgery*, 25(2), 91-95.