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Abstract
The field of cosmetic dentistry emerged when people began to realize the importance of a good smile. Stains on teeth were no longer deemed acceptable with the advent of cheap and safe procedures like tooth bleaching. This new procedure replaced the older, more costly and invasive method of laminated veneers and crowns. The chemistry behind this bleaching occurs via unstable hydroxyl radicals and thus the question arose as to how safe this accepted procedure really is. The purpose of this paper is to analyze the negative ramifications of tooth bleaching and to determine if it's truly safe. The null hypothesis is that the procedure is innocuous and the status quo of cosmetic dentistry is appropriate. Data for this report was obtained from EBSCOhost, Google scholar and PubMed. Tooth sensitivity, oral mucosal and gingival irritation are among the most common side effects observed. More serious side effects like weakening of bond strength, leakage of restorations, cervical root resorption, bleachorexia and degradation of enamel matrix are all observed and are concluded to be serious issues. Though they are reported in the literature, carcinogenicity, mutagenicity and depletion of oral microbes are all determined to not be of any true concern. With a plethora of reasons to avoid tooth whitening, it's imperative that users be properly informed before commencing whitening. This will ensure that all possible measures to avoid these negative effects are indeed taken. Needless to say, the use of such toxic materials shouldn't be available OTC (over-the-counter) as they currently are. If a new and cheaper system is developed on the heels of the successful Pearl Brilliant White Ionic Teeth Whitening System, then bleaching will finally be a safe and universal procedure.

Introduction
In many social circles a good smile is considered indicative of a healthy lifestyle and a wholesome person. Anthropologists have shown that people with striking smiles are more successful and confident than their peers (Townsville Bulletin, 2005). It has been noted that the biggest indicator to a smile's importance is the recent surge in purchase of whitening products and the reading of articles pertaining to such goods (Kihn, 2007). By nature, most people have a low self-esteem and will do anything to gain confidence in themselves or others. This is the root cause for the recent popularity of whitening procedures being used by adults to restore their original white tooth shade.

Most people are born with the potential for untainted white teeth, yet when they reach their adult years this doesn't become the reality. What happened along the way to change this potential? The answer is that their teeth became stained in one of two manners, intrinsically or extrinsically. Extrinsic staining occurs when the enamel of the teeth is discolored by intensely colored pigments termed chromogens that possess ability to bind to its white, outer portion. Coffee, red wine, cola, and tea all have these chromogens and contribute to extrinsic staining. Smoking is another lead cause as the tobacco is composed of two different key components. Tar is naturally dark and promotes staining, while nicotine is colorless. However, when the nicotine is mixed with oxygen it becomes a yellowish surface staining material.

Intrinsic staining is an entirely different subject and is the result of a discoloration of the internal structure of the teeth, known as the dentin. Dentinogenesis imperfecta is a genetical disorder of tooth development which causes improper dentin formation and results in teeth that may take on a blue-gray or yellow-brown hue. Both deciduous and adult teeth are subject to this malady which may weaken teeth more than normal, making them prone to erode, break, and even become permanently lost. Although fluoride is necessary to help prevent decay, if taken too far and ingested in excessive quantities it can lead to fluorosis. Fluorosis will result in white streaks that appear on the teeth and can only be removed with dental measures like bleaching. Trauma to the teeth can either cause internal bleeding discoloration or alternatively lay down more dentin under the enamel layer. As a result of dentin being a darker shade than the enamel layer, the darkness shows through and gives off a darker appearance. Another source for internal staining is tetracycline staining. The minocycline binds to plasma proteins and becomes deposited into the collagen-rich connective tissues of the bone, teeth and pulp. It starts with a light yellow tinge and develops into stronger colors when it oxidizes upon exposure to light (Good, Hussey, 2003). Finally, the most prominent cause for the odd tone of teeth is the indefatigable age factor. As people age, their enamel wears thin and reveals the yellower dentin beneath it. All of these causes can lead people to seek change and investigate the subject of tooth whitening.

The tooth whitening that will be dealt with in this thesis is far more effective in removing extrinsic stains than intrinsic ones. Tooth whitening by definition means the reestablishment of the initial and natural color of the tooth, while tooth bleaching is going beyond that which is natural. However, being that the terms are used interchangeably in varying circumstances and throughout the literature, the same pattern will be followed here. Both whitening and bleaching will thus always be referring to the general color change, without discussing its earlier appearance. Furthermore, it must be pointed out by way of introduction that prior to bleaching, the way to change the color

of teeth was via laminated veneers or crowns. The invention of tooth bleaching was designed to be a more cost-effective and less invasive procedure.

The mechanism of the bleaching isn't fully understood but the principle concept is almost universally accepted. The active ingredient is either HP (hydrogen peroxide), or CP (carbamide peroxide) which breaks down into 33% HP and is thus a weaker version of the former. An oxygen species which can vary between perhydroxyl anion (H02-), hydroxyl radical (HO-) and various other radicals subsequently forms from the HP. The structure of the radical depends on the reaction conditions such as presence of transition metals, light, temperature and pH (Joiner, 2006). This radical reacts with the extracellular matrix portion, specifically the chromophores and pigments it contains, to degrade the stains formed on the surface of the teeth (Goldberg, et. al. 2010). The chromophores are the part of the molecule of a dye that is responsible for its color, while the chromogens are those substances that can be converted into a pigment or dye. In a broader sense, it can be said that HP or CP break stains into smaller pieces, making the color less concentrated and consequently the teeth brighter. In a more technical chemistry sense, it can be said that the reaction with HP or CP leads to the oxidation of carbon double bonds in organic chromogens. This in turn fragments the chromogens so that the power of their color is subdued or even eliminated (Carey, 2014).

A study aimed at determining the relative effectiveness of CP or HP tested six people, having three of them perform bleaching with 3.5% HP and the other three by using 10% CP. These two concentrations are equivalent, as the more complex CP molecule breaks down into 33% HP and 67% other materials. Comparing results by using the Vitapan Classical shade guide to test the percentage of color change, the two substances were deemed to be statistically similar. Canines and incisors both decreased a few shades despite the fact that the concentration of peroxide was on the lower side of the bleaching spectrum in both cases (Berga-Cabarello et. al. 2005). Although the sample size was small, it is sufficient as it is merely confirming that which was previously understood as common knowledge. It can be seen from this study that pure HP is a more potent whitener than CP, as CP requires three times the concentration for equal results. However, it has been postulated although not yet proven, that CP does have its own advantage over HP. Equivalent amounts of oxygen species are released in both HP and CP, but not in equivalent amounts of time. CP releases the oxygen species slower and is consequently more stable, yielding better long-term results. Due to a lack of experiments on this theory, further testing should be performed to substantiate this claim about the long-term results.

There are three methods of bleaching that effectively remove most extrinsic stains and some intrinsic ones as well. Whitening toothpaste isn't among these three as it is only effective for light surface stains. The first is the power bleaching method performed chairside by a dentist. It requires usage of a high concentration of bleach (usually between 30% and 38% HP) and is applied for a duration of 30 minutes to an hour. During such a procedure, the dentist creates a seal around the bleaching area to ensure that the highly-concentrated bleach doesn't end up being ingested or in contact with the gums and thus irritating them. A second method is the supervised take-home method that is also monitored by a dentist. First, the patient visits the office to create molds for the teeth that will be used for the treatment. Then the peroxide is given in a gel form to be placed in the trays and applied at the dentist's recommended concentration. This is usually between 10% and 20% CP (equivalent to 3.5% and 7% HP respectively) and involves duration of a few hours daily for a couple of weeks. Periodic complementary appointments at the dentist's office are recommended to ensure the success of the operation. A third method is the OTC (over-the-counter) bleaching method. The user can find these whitening strips or gels at their local pharmacy or even on the internet. The concentration of peroxide in OTC products is in the 5% to 7% HP range.

The advantage of the chairside power bleaching is that it can be done at a rapid speed, with high concentrations, expediting the bleaching process. Its higher price tag, requirement to visit an office for treatment and use of dangerous concentrations of powerful chemicals makes some people wary of its usage. OTC products are far cheaper and can be done at the user's convenience, however the lack of professional regulation makes some people hesitant to employ it. Furthermore, it can get messy and is less effective for strong stains, making some people question if it's worth the bother. The take-home method is moderately priced and is the intermediate between the fully regulated power bleaching and the more controversial OTC products.

A study was performed to compare the color change and rebound effect of power bleaching in comparison to take-home bleaching. Rebound effect is a measure of how quickly the results of the whitening fade and the initial discoloration returns. A split mouth design was used where twenty patients were randomly assigned chairside bleaching to either their mandibular or maxillary anterior teeth and then followed by take-home bleaching to the other. Excluded from this study as well as all other studies listed in this thesis were those with active caries, periodontal diseases, previous bleaching procedures and orthodontic treatments. Additionally, those with tetracycline-staining, fluorosis and those who habitually smoke were omitted. This ensured that the results would be a direct indicator to the effectiveness

of bleaching to standard patients with regular extrinsic stains, and not tainted by outside factors during the treatment time. Patients were evaluated by a single examiner, blinded to each patient's bleaching regimen, immediately after treatment and 2 weeks, 1 month, 3 months and 6 months later. The testing was done to measure for bleaching effect, rebound effect and color difference between post-treatment and unbleached teeth. The results showed that there was no significant difference between power bleaching and take-home whitening on any of the matters being evaluated except for rebound effect at the 6 month follow-up. While take-home whitening didn't have a distinguishable rebound effect at 6 months, the power bleaching did. This can be explained by the dehydration effect that power bleaching has on the teeth, which will interfere temporarily with the evaluation of color differences. It can be said that a lot of the color improvement associated with power bleaching is an illusion caused by this dehydration effect rather that an actual improvement in the tooth shade. Another explanation is the longevity of treatment. Take-home bleaching is continuous for two weeks which allows for bleaching demineralization to work together with natural remineralization and results in longer lasting effects. However, power bleaching is a one-time treatment and thus remineralization begins right away, resulting in faster regression of the whitening effect. Although regression occurs faster in the power bleaching, there is no overall statistical difference in the color comparison of post-treatment teeth and those untreated (Moghadam, et. al. 2013).

More recently, it has been suggested that the use of laser heating can enhance the effects of tooth whitening. Regular whitening without heating works because the peroxide releases hydroxyl radicals that diffuse into the outer enamel and break down the stains in a matter of hours. Lasers can heat the HP and expedite the chemical reaction that leads to radical formation, reducing bleaching time. However, despite the popularity of such heating devices, it really has no effect on the quality, durability or speed of the bleaching (Carey 2014). Although there are those who argue and that it does work faster, it is still more costly and has reportedly increased the subsequent tooth sensitivity. It can be concluded that the results of light-activated procedures are equal to those lacking such treatment and there is no real benefit to using such methods (Kihn, 2007).

A study was performed using third molars to test the effect of various concentrations of bleaching substances on the degree of whitening. Hydrogen peroxide of 5, 10, 15, 25 and 35% concentration was applied to test the degree of whitening each one would do in the same 3 x 10 minute sessions. Unsurprisingly the 35% HP was the most effective, while the 5% was the least effective in changing tooth shade. Furthermore, the 35% HP reached the maximum degree of whitening in just one session, showing that it's the fastest method. However, the 5% HP took a staggering 12 sessions to reach the same maximum shade. The expectation was that the relationship would be linear and that 5% HP would require only 7 sessions to equal its 35% HP counterpart. Instead, results showed that the number of sessions increase exponentially with lower concentration and that the relationship isn't merely linear. An explanation for this phenomenon is that tooth whitening is far more complex and involves numerous factors to attain the same results. Thus, the diffusion and reaction of the degraded components of the peroxide with chromogens may not work under expected patterns. Despite this strange peculiarity, once the maximum shade is reached, there is no difference between the higher and lower dosages of HP with regard to its longevity (Sulieman, et. al. 2004).

As is the case with most medications and procedures, tooth bleaching has its fair share of side effects. Is tooth bleaching really as safe as advertised? Are potential by-products transient or are their effects felt over the long haul? The null hypothesis prior to investigation of the subject is that there are no serious negative results to tooth bleaching, regardless of technique. The procedures are ADA approved and it's unlikely they would sanction the use of unsafe methods. Furthermore, the technique has been in use for many years and if it was really harmful, would undoubtedly have been banned by now.

Methods

Data was found using a variety of different internet sources. PubMed and EBSCOhost were very helpful in providing data. Additionally, Google Scholar was used as a powerful search engine.

Discussion

Dentin hypersensitivity (mostly thermal) is the cause for the aches and pains associated with tooth whitening. Increased sensitivity is the most common by-product and some degree has been reported in over 50% of patients (Jorgensen, Carroll, 2002). A survey reported that 78% of tooth bleachers experienced pains of some sort ensuing their bleaching regimen. The chemical process for whitening releases the dentinal plug that is thought to be protecting the region. With the plugs removed, the core of the tooth becomes exposed to things from which it is usually safe. A dentinal fluid flow occurs internally, as a result, and leads to the excitement of pulpal tissue and the consequent sensitivity.

There are two ways to counteract the sensitivity created by removal of the dentinal plug that accompanies tooth whitening. One method is to replace the dentinal plug by using dental sealants to cover the exposed root. Varnishes, bonding agents, and restorative materials are all viable ways to physically close the gap. Another related way is to commence the usage of fluorides which will decrease the permeability of the teeth. A different

approach is to cause depolarization of the nerve. Application of 5% potassium nitrate can cause a soothing effect on the nerve. It acts as a tranquilizer and slows the repolarization, which in turn eases the pain that is associated with the irritated nerve.

An experiment was conducted to compare the tooth sensitivity experienced in at-home bleaching with 10 and 20% CP vs. in-office power bleaching with 35 and 38% HP. Twenty-five patients for each of the four categories were gathered for this experiment. The at-home treatments were accompanied by the antidotes of potassium nitrate and fluoride to see if they would help. Tooth sensitivity was measured qualitatively, as each week the patients were asked if pain was absent, mild, moderate or severe. Thirteen percent withdrew with pain they deemed intolerable, showing that not all pain involved was so temporary and bearable. The results dictated that 43.2% of patients experienced pain, which fits well with Jorgensen and Carroll's results in 2003. The puzzling statistic was that a high volume of 71.4% of users of 20% CP experienced pain. This phenomenon was astonishing considering that only 15% of those power bleached with 38% HP experienced the uncomfortable sensation. As a whole, 9.5% from the take-home treatments in comparison with 4.3% of the in-office whiteners felt the sensation (Basting, et. al. 2012). This experiment indicates that there are other factors besides concentration that play a role in causing tooth sensitivity. Had it been solely based on concentration, then the chairside whiteners would have endured more sensitivity than their counterparts at home. Perhaps it can be concluded that the duration of the take-home bleaching made up for its lack in concentration. Another disappointing conclusion was the minimal effect that remedies like fluoride and potassium nitrate had on quelling the pain.

The split mouth design experiment also tested for tooth sensitivity and is important in regards to comparing sensitivity of at-home treatments vs. in-office power bleaching. At all the time intervals that color change was measured, tooth sensitivity was assessed by use of a visual analog scale. The results showed no significant difference between the two types of whitening treatments as each reported sensitivity in the 40-60% range. Using standard deviation this is deemed statistically insignificant and thus both were considered to be equally irritating (Moghadam, et. al. 2013).

Another adverse by-product of bleaching is the oral mucosa irritation that will occur if not applied properly. Oral mucosa is the mucous membrane that covers the entire inside of the mouth with the exclusion of the teeth. This protective membrane helps maintain oral health and is composed of strong keratin fibers which makes it resistant to injury. At a concentration in excess of 10%, HP is deemed to be corrosive to the mucous membrane and can cause burns and tissue damage. When power bleaching is performed it's imperative that there be something that holds back the highly potent peroxide from entering the oral cavity. Furthermore, patients shouldn't be numbed during such procedures, as they must be able to alert the practitioner in the event they feel a burning sensation (Li, 2011). However, a patient's perception of pain can't be relied upon and the dentist must constantly check the adequacy of the barrier that was constructed. It would be prudent to use some form of dyed substance to test how the barrier really is. If no die leaks through, it can then be considered safe enough to proceed with the whitening procedure.

A related issue is the gingival irritation that often occurs post-bleaching. Gums are a soft pinkish tissue that is composed of oral mucosa, and is vital in supporting, surrounding, and protecting the teeth. Issues with gums have been linked to cardiovascular and respiratory disease by some health professionals. Therefore, it is highly alarming that patients who have undergone whitening treatment have in certain cases developed gingivitis. This inflammation of the gums will lead to red and swollen gums that tend to bleed easily. The onset of gingivitis occurs because gums, like all oral mucosa, are subject to damage at concentrations exceeding 10% HP. The cause for gingivitis is an ill-fitting tray or a leaky and failing barrier during office whitening treatments. Although mucosal irritation is often temporary, gingivitis is a dangerous disease that must be taken into account when balancing the merits and dangers of whitening. With such dangers lurking, it's quite clear that such substances shouldn't be placed in the hands of minors or irresponsible people.

An interesting study of an innovative OTC bleaching tray system helps shed some light on the mucosal and gingival irritation that often accompanies whitening. Thirty-eight subjects were provided with the Pearl Brilliant White Ionic Teeth Whitening System which contains 9% HP and uses electrodes in the wall of trays to deliver an electrical current. The 4-15 milliamperes current activates the gel, causing it to diffuse through the enamel, and leads to the oxidation of pigments and chromophores that is standard in all whitening methods. The purpose of the electrical power is to speed up the formation of radicals and thus reduce application time of trays. The 38 patients applied the trays twice daily for five minutes and a mere five days. This contrasts with standard OTC strips which must be worn for excess of an hour per application and multiple weeks per cycle. Patients were checked after the first treatment and after five days for irritations, sensitivity and for effectiveness of the bleaching protocol. Results after the first treatment reported a mean improvement of 2.3 shades and only 20% discomfort, with two patients reporting slight burns of oral mucosa. After five days, only 15% of patients reported any discomfort and nobody had to stop treatment early. The average gingival score didn't have a significant change and there was no additional inflammation after application of

the gel. Only seven of 38 patients had any blanching of oral mucosa during any point of the treatment, and such side effects lasted just a few minutes and didn't require intervention. The results showed a sharp contrast between the electric powered tray system's 20% discomfort level and standard OTC whitening strips 50% sensitivity incidence (Ghalili, et. al. 2014)

The cause for the lower sensitivity and irritation prevalence may have been a result of the addition of potassium nitrate to the HP gel which slows repolarization of the nerve and lessens the pain. However, it was shown in an earlier experiment that such treatment doesn't necessarily work (Basting, et. al. 2012). A more likely explanation is the decrease in wearing time of trays and contact time of the peroxide gel. These results and accompanying explanation would fit well with the conclusion that was made earlier regarding that experiment, where it was stated that increase in duration of bleaching can lead to increased sensitivity. The usage of this novel OTC treatment is slowed by its heavy price tag of $200 per tray, but its prowess is important to note. If time can be reduced significantly in an affordable manner, then many of the main side effects of bleaching will disappear.

The most harmful effect that any substance can have is carcinogenicity, the ability to cause cancer, primarily by genotoxicity. Genotoxicity is the negative effect that harmful substances can have on the genome by causing mutations to the cell's DNA. The method for testing for genotoxicity is via a micronucleus test that quantitatively measures chromosomal damage by counting all cells that have inducted micronuclei into their cytoplasm after exposure to genotoxic agents. These micronuclei form when all or part of a chromosome isn't incorporated into a daughter cell during cell division. A high micronucleus count is indicative of severe chromosomal instability and genotoxic effects that pose a health risk. The DNA fragments will occur only in those cells that have completed one round of cell division after exposure to the genotoxic agent. The lack of incorporation of the micronuclei is due to a lack of centromeres that prevents the fragments from migrating to the spindle poles during late anaphase. The end result is that fragments are left behind and they form a secondary nucleus that is kept in the cell cytoplasm.

When compiling a list of the drawbacks to tooth bleaching, the potential correlation to genotoxicity and carcinogenicity must be thoroughly investigated. The theory had been proposed that HP may raise the carcinogenic effect, much like it does in experimental animals. However, it has also been argued that those artificial conditions are of no relevance to tooth bleaching, as they have much higher levels of HP than tooth bleaching does. A study was performed to find the genotoxic effect of 10 and 16% CP on bleached patients. Particularly concerning is the presence of reactive oxygen species in the peroxides that could damage proteins and cell nucleus. Thirty-seven patients were randomly divided into two concentration groups and given customized trays to wear for two hours daily for a duration of three weeks. Collections of gingival margin cells were taken at baseline, 15 days and 45 days by abrasion and then properly affixed to slides. One thousand cells were counted per slide and underwent a micronucleus assay. Comparing the results of the 10 and 16% CP there was no statistical difference between the rates of micronuclei formation at all three time periods. Most importantly, the rates were in fact on the lower end of the 0.3 to 1.7% range given in previous experiments (Bona

ssi, et. al. 2011). These results showed that when not applied for long periods of time or improperly consumed, the use of peroxides alone isn't cytotoxic. Hence it can be concluded that teeth bleaching doesn't pose a threat to human gingival epithelial cells (Almeida, et. al. 2015).

Another study corroborated the results of the previous experiment. Thirty smokers and thirty non-smokers were given 10% CP to be used three hours daily for three weeks. The goal of this single-blind trial was to compare the genotoxicity and efficacy of at-home whitening between smokers and non-smokers. The usage of a micronucleus assay is a good indication of cancer risk associated with genotoxicity, as most tumors in humans originate in the epithelium. The results indicated that bleaching didn't increase the frequency of micronuclei in the cytoplasm. The number of micronuclei was higher in smokers than non-smokers, but that was the case prior to baseline (the starting point used for comparisons). This is merely indicative of the genotoxic effect of habitually smoking, and is unrelated to its effect on bleaching. Smokers and non-smokers alike didn't have a significant increase in micronucleus formation after performing bleaching. Ten percent CP was thus proven to be safe when used at low concentrations for the three-week period that was required. The study did have limitations as it wasn't truly a blind examiner that was testing for genotoxicity. The smokers had a stench on their clothing and in their breath, giving away the identity of the group to which they belonged. Furthermore, the timing of the post-bleaching micronucleus assay wasn't optimal as it was given shortly after the whitening treatment. In contrast, the regeneration of the cells from gingival tissue takes approximately ten to twelve days. Thus, had the assay been performed two weeks later it's possible the results would have changed (de Geus, et. al. 2015). However, the limitations can be overlooked as the results are backed by other studies (Almeida, et. al. 2015).

A consensus opinion on the matter of genotoxicity and carcinogenicity is given in a recent review article. Direct contact with peroxide can cause genotoxicity in cultured cells and bacteria. However, when in the presence of catalase and other biological

enzymes, the effect is mitigated. The free radicals of the reactive oxygen species need to reach the DNA to inflict damage and the presence of metabolizing agents inhibits their ability to reach the target in vivo. Thus, while it is a threat to bacteria in a lab, in humans it isn't deemed a real threat. HP has a weak local carcinogenic potential and nothing more. The International Agency for Research of Cancer put HP in group three as unclassifiable in its carcinogenicity in humans. Most certainly, the mild dose of 10% CP found in many at-home trays is of no threat to those not already predisposed to oral cancer (Perchyonok and Grobler, 2015).

There was one case trial that did experience a higher rate of mutagenicity as a result of using tooth whitening in vivo on humans. Two different groups received different types of in-office bleaching. The first group used ZOOM2, a 25% HP that also features light activation. The second group received Opalescence BOOST, a 38% HP which had no light treatment. Cell samples were collected from both the upper lip lining and the gingival area, via swab technique. Each sample was collected before bleach application, immediately after and then 72 hours post-whitening. The collection immediately after bleaching was a control group, as there wasn't enough time for mutant cells to reproduce and appear in the results. The collection 72 hours after treatment was the experimental group, as that is ample time for reproduction of cells. Although there were only eleven members in each group, the design was to capture large effects and for this purpose Cohen's size conventions test determined that eleven was large enough.

Results showed slightly higher indicators of genotoxicity in BOOST, but both forms of bleaching caused a large increase in these markers. When comparing the control and experimental groups, BOOST saw a 157% increase in micronucleus presence while ZOOM2 experienced a 142% hike. These results contradict those of other studies, however, there are numerous explanations to reconcile the differing conclusions. The aforementioned experiments headed by both Almedia (2015) and de Geus (2015) used low concentrations of CP, while this experiment used high concentrations of the stronger HP. This may have led to the genotoxicity increase and wouldn't be indicative of issues in at-home bleaching. Furthermore, even power bleaching isn't necessarily problematic as there were flaws in this experiment. Five out of 22 patients had minor restorations which is usually grounds for exclusion, as they have a negative effect and increase the micronucleus count. Also, patient's lifestyles can't be controlled and while in other experiments they may have refrained from negative behaviors, this experiment may have been an exception. Alcohol usage and improper diet have been linked to an increase in micronucleus count. All of these explanations make this case seem as more of an aberration than a rule (Klaric, et. al 2013).

Tooth whitening can cause permanent damage to the enamel structure. In addition to the free radicals, CP produces urea which subsequently decomposes into CO2 and ammonia. This is key in the bleaching process as the urea degrades the organic matrix in the enamel. Hydrogen bonds in matrix proteins are dissociated by the urea and ammonium ions. These empty spaces caused by the degrading of matrix proteins make possible for penetration of the free radicals to enamel and even dentine layers. However, whatever breakdown the urea creates is in fact real and permanent damage to the enamel and is one of the more serious issues of tooth whitening (Elfallah and Swain, 2013).

While enamel erosion is a serious issue, it has become well publicized that remineralization agents are a viable method for restoring tooth structure. An experiment was conducted to test enamel erosion generated by two different high concentration HP whiteners. Opalescence BOOST was used as a substance that is chemically active, while Mirawhite is a 30% HP substance that is activated by a diode laser. The experiment also tested four different remineralization agents to see which would be most effective in restoring initial tooth structure. Twenty-five molars for each whitening type were each subdivided into five groups, which featured one control group and four different remineralization experimental groups. The exact statistical measures for erosion and remineralization are unimportant, but the generalizations were quite startling. SEM/3D-SEM-micrographs revealed that both types of bleaching caused emphasized perikymata, which are the pits surrounding the long prisms of tooth enamel. These emphasized perikymata as well as the loss of interprizmatic substance both clearly indicated enamel erosion. These negative signs were even exacerbated in the teeth that were activated by the diode laser. Remineralization occurred in all four experimental groups, with calcium phosphate proving to be the best at covering the surface of the enamel. SEM/EDX-semiquantitative analysis showed that certain crucial elements were reduced from the tooth structure as a result of the bleaching procedure. Sodium and magnesium were most prolifically lost in the non-laser bleaching, while calcium and phosphorus were the hardest hit by the laser bleaching (Coceska, et. al. 2016).

Although remineralization agents can help repair the erosive effects of bleaching, this only works if patients are properly informed to commence application upon the onset of whitening treatment. However, users of OTC products are generally not properly informed and also further their plight by not reading the instructions. Thus, even when side effects are indicated in the user's manual, most consumers remain oblivious to the need for these remineralization agents. The loss of enamel causes a decrease in insulation from potential painful temperature and dangerous chemicals and can also lead to decay. Furthermore, enamel erosion makes the tooth more prone to chipping. Once

the enamel is lost it has no living cells to repair itself. All damage is permanent and costly alternative treatments such as bonding are now required.

The leakage of restorative materials ensuing tooth whitening is another major by-product of the procedure. Restorative materials have been used for many years to fill caries, repair damage due to trauma and much more. Originally amalgam was the primary restorative material, until a recent surge in the use of composite resin material. Issues arise when there is a leakage of mercury ions from amalgam upon the initiation of bleaching. Mercury ions can be toxic and lead to numerous diseases when the threshold concentration is reached.

The amalgam's natural release is a redox (oxidation-reduction) reaction in which the mercury metal reacts with non-metallic elements to produce chemical compounds (von Fraunhofer and Staheli, 1972). This same reaction would take place in vitro, as the redox reaction takes place at the amalgam/bleach interface resulting in the deposits. An experiment was thus conducted to investigate how much of a role both concentration and time of treatment have on the release of mercury. Tytin amalgam contains 42.5% mercury and is a typical dental restorative material. Sixty-five discs of tytin amalgam were prepared and divided into thirteen groups of five for the experiment. Four groups of discs were each treated with 0%, 3.6% and 6% HP. The various groups had varying times of exposure to HP of 1, 8, 48 and 156 hours respectively. The 0% HP groups were the control groups and contained saliva and other biological enzymes in place of the peroxide. The 3.6% HP groups represented the classical at-home concentration and the 6% HP represented a stronger version of these groups. The various times made this into a double experiment that charted both concentration and time of exposure against amount of mercury ion leakage. The thirteenth group was treated with 30% HP for one hour and was an imitation of in-office power bleaching. Each disc was measured five times for amount of mercury ion release and each group had five discs to ensure the accuracy of the measurements.

The results showed a greater release of mercury ions as the concentration of bleach was increased. Time caused increased release until the eight hour mark, at which point its effect plateaued. This showed that concentration was of greater effect than time and thus power bleachers should be cautious before starting whitening. However, the small amounts of mercury released don't produce effects on humans, as the quantities are well below the acceptable daily intake of forty micrograms. The maximum sum released by any of the discs was 1.125 micrograms and thus would require 36 teeth with restorations to pose any threat. Despite its relative safety, it's still not healthy to have any amount of harmful chemicals in the body and thus the release of amalgam is a side effect that must be taken into consideration when considering bleaching. In fact, this danger has caused Norway to ban amalgam restorations now that safer alternatives are available (Al-Salehi, 2009).

Scientists hypothesized that upon the onset of bleaching, an additional consequence would result from the redox reaction that occurs at the dentin. They feared bond strength at the dentin/resin interface would be adversely affected. To confirm this suspicion, they performed an experiment to test all facets of bond strength after application of varying concentrations of bleach to teeth. For the shear bond strength test, forty slabs of intracoronary dentin were obtained and split into four groups. One was a control group that was treated with artificial saliva that had no HP concentration. The second group was 20% HP and also had sodium perborate (a bleaching agent), a third group was comprised of 37% CP and a fourth group of 38% HP. Manufacturer protocol was performed for all bleaching regimens and a seven day waiting period ensued as a means to offer appropriate time for the residual bleach to leave the dentin. These teeth then received a shear bond strength test in a universal testing machine. Failure modes for the test were observed via microscope. Next, a flexural/fracture strength of dentin test was done on forty dentin bars from the cervical area of the buccal portion of roots. These forty bars were divided into the same four groups, underwent the same treatments and then received a three point test carried out by a universal testing machine. Finally, an SEM analysis of dentin surface and adhesive interface was prepared with five hemi-sections of lingual surface of crowns, for both the dentin surface and adhesive interface.

The results showed that shear bond strength of the control group was nearly double to that of the experimental groups. The unbleached teeth had mixed failure modes of both cohesive and adhesive failures, while the bleached groups had predominantly adhesive failures. Flexural strength was statistically significantly higher for the unbleached group than the experimental groups. The 38% HP was the weakest of all groups, although it was statistically similar to the 20% HP coupled with sodium perborate. Lastly, unbleached teeth had SEM analysis that showed dentin surface covered with its smear layer, the two middle groups had some areas with fissures and the 38% HP sample had cracks all over the specimens. Analyzing dentin/material interface there was a continuous interface in the unbleached group, and progressively more discontinuity areas with the higher concentration bleached groups.

The explanation for the weaker shear bond strength in bleached groups, is that hydroxyl radicals penetrate into dentin and break down connective tissue, such as collagen and hyaluronic acid. This in turn increases dentin permeability, reduces hardness and

leads to the decrease in shear bond strength. The oxygen inhibits the entrance of the resin/material into dentinal tubules and prevents their polymerization. Even after seven days, residual oxygen remains and causes adhesive failure. Hence, the analysis of failure modes indicated more adhesive failure for bleached teeth, while unbleached teeth had less adhesion failure modes and instead more cohesion failure modes. This furthers the notion that hydroxyl radicals formed from bleaching products interferes with the bonding of restorative materials. This may also be a secondary reason for leakage of amalgam restorations, as the failure to properly bind at adhesive interface causes the subsequent leakage. The SEM results were consistent with those of the shear bond strength test, as those with the highest HP concentration had more cracks in the dentin surface than those with lower HP. Finally, the flexural strength test confirmed the scientist's fears, as those with higher HP had less strength and would thus fracture faster in-vivo. All of these test results can be explained with the common theme, that the hydroxyl radicals ruin the structure of teeth while also reducing the ability of the resin to properly bond to the dentin (Vieira, et. al. 2012).

There have been numerous mechanisms proposed as ways to reduce and prevent the microleakage of composite resin restorations. This microleakage is particularly common when bleaching is done just prior to or soon after installation of the restoration. The bleach leaves behind residual peroxide that doesn't allow for proper polymerization of the resin to the remaining portion of the natural tooth. A test was done to compare various suggested means of mitigating the microleakage effect. Sixty intact premolars were split into six groups for the purpose of this trial. Group one was the control group, as the teeth were merely treated with saliva instead of the 10% CP applied to other groups. There has been a theory that allowing a three week time delay between bleaching and bonding would be ample time to allow residual peroxide to dissipate out of the teeth (Bittencourt, et. al 2010). Thus, group three was treated with 10% CP followed by a three week delay before installation of fillings. Group two provided the proper contrast to group three, as it was treated with 10% CP and didn't have the deferral of restorations found in group three. Group four had sodium ascorbate applied in between bleaching and the filling of caries. This chemical is an antioxidant and was seen as a faster alternative to the potentially equally effective but highly time consuming delay period. A recent study suggested that addition of surfactant (0.2% Tween 80) would enhance sodium ascorbate's ability to prevent microleakage (Moosavi, et. al 2010). Thus, group five presented sodium ascorbate coupled with surfactant treatment between bleaching and restorations. Finally, group six was treated with catalase instead of the antioxidant and surfactant, following a report that catalase removes residual HP from the surrounding area after bleaching (Rotstein, 1993). Microleakage was measured semi-quantitatively by the accepted criteria of the depth of dye penetration at the interface between restoration and cavity wall.

Data from the trial indicated a significant difference in amount of microleakage between the unbleached group one and bleached groups two through six. Furthermore, group two had the greatest microleakage as it had no preventive measures implemented preceding addition of composite resin. Groups five and six, although significantly greater in microleakage than group one, was significantly less than group two. It is thus evident that sodium ascorbate in conjunction with surfactant and catalase by itself are a sufficient method of reducing (but not completely terminating) composite resin microleakage. Groups three and four were statistically similar to group two, showing they were relatively ineffective at preventing microleakage (Han, et. al. 2014).

Extending the theory that explained the results found in this microleakage experiment, one can opine that application of catalase can also help cure the woes of the weakening of bond strength caused by whitening. This in fact concurs with a previously performed experiment which also concluded that pretreatment of bleached surfaces with catalase prior to bonding improves composite-enamel bond strength (Kum, et. al. 2004). On the surface this seems very reasonable, as one of the causes for both microleakage of restorations and weakening of bond strength, is the oxidative materials left behind after bleaching which prevents polymerization of installed materials to the natural tooth. If catalase can serve as a deterrent to microleakage it should then follow that it should relieve the stress on bond strength that the same residual harmful materials cause. However, catalase wouldn't be of any help for other side effects mentioned earlier in this report, as those aren't a result of the residual oxidative materials that the bleach leaves behind.

Cervical root resorption (reabsorption) is a naturally occurring process in primary teeth, as the deciduous teeth are uprooted to make way for the permanent teeth. This process is caused by the osteoclast differentiation that results from the pressure applied by the newly emerging teeth. However, as a result of trauma or excessive pressure of various orthodontic treatments, it's possible for a pathogenic resorption/breakdown of permanent teeth to occur. Such a condition can ruin a tooth if not properly treated. The problem is that this phenomenon is painless and unless detected via x-ray will go undiscovered until after carious lesions have taken hold in the external tooth. Bleaching is one of the orthodontic treatments that is a root cause for resorption due to the pressure associated with it. The disease is more commonly observed in those using HP bleaching than those using sodium perborate alone (Fearon, 2007). Sodium perborate is a milder procedure with less side effects, but shorter sustained

results. Thus, the intensity of the bleaching regimen clearly has a direct effect on likelihood of cervical root resorption. Use of heating devices is another catalyst for this malady. This is a logical consequence, as the heat generates hydroxyl radicals from the HP which are highly reactive and subsequently break down connective tissue found in teeth. Together, high concentration HP and heat can be a lethal combination for those trying to preserve their teeth. Another explanation why bleaching causes root resorption, is that the acidic environment that the bleaching procedure supplies enhances the disease (Dhillon, et. al. 2011). The diffusion of hydrogen ions from the bleach makes the region more acidic and creates an environment that is ripe for bone resorption and osteoclastic activity. The proof to this theory is that osteoclastic activity is strongest in 35% HP (3.7 pH), intermediate in 35% CP (6.5 pH), and weakest in sodium perborate (pH 9.9), a basic substance (Dhillon, et. al. 2007)

Additionally, it has been suggested that the acidic environment that bleaching creates can adversely affect the beneficial microbes that regularly grow in the oral cavity. It's important to have these essential microorganisms so that when adverse, exogenous viruses invade they are outnumbered and combatted by the symbiotic microbes. The harsh, acidic conditions could prove to be too much for the microbes to handle and thus diminish these protective organisms. Such a chain of events would leave whitening users with a greater risk for microbial disease. Four groups of eight were generated to test the effect various treatments and combinations of treatments would have on the overall concentration of microbes in saliva. The results would be a direct indication of the overall concentration in the oral cavity. The first group was treated with in-office CP 37% and at-home CP 10%. The second group received the in-office CP 37% and an at-home placebo, the third group an at-home 10% CP and an in-office placebo, and the final group a double placebo. All patients were given uniform brushes and dentifrices and inasmuch as possible were left under similar conditions. The in-office bleach was conducted in three sessions of one hour and the at-home whitening was three weeks in duration. Saliva was taken at baseline, right after application of bleach, twelve hours later and repeated each week during treatment. The results were placed on various culture media, but all results showed no significant difference between microbial levels at various periods. Thus, it was concluded that the bleaching of teeth has no effect as an antimicrobial agent (Franz-Montan, et. al. 2009).

The final major side effect of bleaching teeth is the potential to develop an addiction to the bleach. Such a disease is known as bleachorexia and those afflicted are dubbed bleachorexics. Much like anorexics who are convinced they aren't skinny enough, bleachorexics are convinced that their teeth aren't white enough. Instead of accomplishing a nice hue, these fanatics whiten to the point where teeth reach a translucent blue or grey appearance. This looks unnatural, especially when contrasted by a person who may have a darker skin tone. Bleachorexia can lead patients to turn an eight week regimen into a full-year program. These tooth whitening junkies present an added health risk with gum, tooth or even throat problems from repeated exposure (Bee, 2006). The relatively recent increase of bleachorexics is due to the prevalence of OTC methods which allows patients to take whitening into their own hands. The enamel becomes permanently damaged, root canal problems arise and free radicals damage cells and pulp in teeth due to the over-indulgence of bleach. Gums may recede, teeth become weaker and all other aforementioned side effects become amplified by the excessive use. Psychological intervention may be required to relieve patients of their plight.

Prior to drawing any conclusions, it's important to examine the long-term effectiveness of tooth whitening. A study was conducted to test for any difference in rebound effect at the two-year mark vs. baseline and the one-week mark vs. baseline. This was done for both at-home bleaching and in-office bleaching, to test which one has more sustainable results over the long haul. The general perception among clinicians has been that the at-home bleaching lasts longer than the in-office bleaching. Results in the split-mouth design experiment corroborated this general view (Moghadam, et. al. 2013). For this experiment thirty patients were given power bleaching for two sessions of 45 minutes during a one-week span. Another thirty patients were given at-home bleaching kits of 16% CP, to be applied for six hours per night for four weeks. Color change was detected using the Vita Lumina shade guide and was measured at baseline, one week later and two years subsequently. Results for at-home whitening showed a mean increase of six shade guide units for both one week and two years successive to bleaching. Rebound effect was 0.25 shade guide units over two years and this was deemed statistically insignificant. The in-office bleaching indicated a 5.5 shade guide unit improvement for both one week and two years after whitening. Rebound effect was 0.30 shade guide units and this too is considered statistically insignificant. Contrary to the common perception, the longevity of results for in-office bleaching was up to par with the take-home bleaching's durability (Tay, et. al. 2012).

The difference between the results of the in-office bleaching's six-month instability in Moghadam's experiment and the two-year durability in Tay's experiment is a simple distinction. In Moghadam's experiment only one session of 45 minutes was given to chairside bleaching patients. In Tay's experiment two such sessions were administered on each patient. According to some experts, it is only after the second bleaching of in-office treatments that tooth color does

change significantly (Al-Shethri, et. al, 2003). Thus, to equal the long-term stability of at-home bleaching, two sessions of chairside bleaching are required.

Conclusion

Although tooth whitening doesn't create a higher probability of carcinogenicity or genotoxicity, it is far from innocuous. Almost 50% of patients experience some form of tooth sensitivity for the first month of treatment. Oral mucosal and gingival irritation are very common as a result of ill-fitting trays and the subsequent leakage of peroxides. Tooth integrity is affected as a result of urea degrading the enamel matrix, and hydrogen bonds in matrix proteins becoming dissociated by the urea and ammonium ions. Due to the redox reaction, there is often an increase in the leakage of restorations, most notably amalgam. Weakening of bond strength is a direct result of the oxygen molecules causing a failure of resin to properly bond to dentin. Cervical root resorption is more likely to occur following the orthodontic treatment associated with bleaching. Finally, there is even a psychological issue named bleachorexia that is caused by a whitening obsession. With this excessive list of side effects it is clear that such dangerous substances must be regulated to some degree and not available over-the-counter as they currently are. It is a travesty that such harmful materials are accessible to minors and are not exclusively in adult's hands.

Various methods have been mentioned throughout the course of this work to help mitigate a number of the by-products of bleaching. While long-term rebound effect is unchanged by the form of bleaching (when power bleaching is done twice), the form of peroxide does matter. CP is said to yield longer-lasting results due to its slower and more stable release of oxygen species. Laser heating doesn't speed up the reaction rate and only serves to increase tooth sensitivity and speed up enamel erosion. Fluoride and potassium nitrate don't mitigate tooth sensitivity but decreasing the application time of bleach certainly can. In fact, usage of a novel electric powered bleach showed that decreasing wearing time can also cause a decrease in gingival and oral mucosal irritations. The best remineralization agent is calcium phosphate and should be taken in conjunction with whitening. Catalase helps remove residual oxygen species and should also be taken while commencing bleaching. The catalase should help relieve some of the woes of weakened bond strength and the leakage of amalgam restorations. Cervical root resorption can be diminished when a lower concentration of peroxide is used and laser treatment is avoided. Thus, the properly informed whitening patient can be shielded from some of the by-products of bleaching if he/she is proactive in treating them. However, the issues arise for patients who are not properly informed or are negligent in providing the proper care for their teeth.

It is clear from the abundance of research provided in this report, that while cheaper, whitening isn't a safe alternative to laminated veneers or crowns. Thus, those who can afford to do so, should choose the more conventional route when looking to make cosmetic repairs on teeth. The future of whitening seems to lie in the ability of companies to create a cheaper system that allows for shorter exposure time to peroxide. The Pearl Brilliant White Ionic Teeth Whitening System which contains 9% HP and uses electrodes in the wall of trays to deliver an electrical current, is definitely a positive start for making this a reality. Ultimately this system needs to be tested more to confirm that it really is effective, while decreasing the side effects. Furthermore, the hefty price tag doesn't allow this brilliant technology to gain enough popularity. A cheaper alternative must be created to allow all members of the populace to have access to this newest advance in the field. Only when this comes to fruition will whitening truly be a safe and cheaper alternative to laminated veneers and crowns.

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