The safety and efficacy of 'over the counter' bleaching products in the UK

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Key points

Describes the range of over the counter (OTC) bleaching products available in the UK.	Suggests advice to give to patients with regards to OTC bleaching products.	Improves understanding of core bleaching concepts and bleaching research.

Introduction EU council directive 2011/84/EU resulted in a demand for over the counter (OTC) bleaching products. The industry has latched onto this renewed demand by developing a range of non-hydrogen peroxide OTC products. **Aims** To determine whether non-hydrogen peroxide OTC whitening products available in the UK are safe and to determine the lightening effect of those products. **Materials and methods** A total of 21 extracted teeth (11 incisors and ten premolars) were collected and stored in chloramine-T solution. Five days before the study, all teeth were immersed in 5 ml of a standard green tea solution at room temperature (22±2 °C). Roots were sectioned from the teeth and cleaned using an ultrasonic bath. Teeth were then embedded in epoxy resin and sectioned inciso-gingivally to serve as paired test and control specimens. A positive control of 10% carbamide peroxide was used while saline was used as a negative control. Five OTC products were selected from two major British consumer outlets. Initially, products were applied to the teeth samples for two one-hour cycles, followed by the equivalent of one-week's application, according to the manufacturer's instruction. Samples were stored overnight in saline to minimise any effects of dehydration. Shades of teeth were taken blindly by a single trained clinician in a natural light environment against a grey background before and after application of the products. Vickers microhardness tests and scanning electron microscopy (SEM) analysis were undertaken. **Results** SEM analysis showed surface morphology alterations to varying degrees, with several samples demonstrating a distinct etching pattern post-exposure to the OTC products. Sample three ('Brilliant 5 minute kit') and sample five ('iWhite instant teeth whitening') produced the most extensive surface alterations. Samples three and five also resulted in a significant reduction ($p = 0.008$) in Vickers microhardness. Two OTC products resulted in a lightening effect less than the negative control saline, whereas two other OTC products resulted in a lightening effect greater than carbamide peroxide. **Conclusion** This study suggests that non-hydrogen peroxide OTC products have the potential to damage enamel and lighten teeth. The lightening effect of the OTC products is variable, however, it is most likely to occur in sodium chlorite based products.

Introduction

Tooth bleaching has gained popularity over the last few years due to the ease at which the treatment can be undertaken and the effect it has on the aesthetics of the smile. This popularity

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has led to the development of an 11 billion dollars per year industry in the USA alone.[1] There is also massive demand for white teeth in the UK and the industry has now latched onto this opportunity.

Traditional whitening agents, especially carbamide peroxide (CP) and hydrogen peroxide (HP), have provided patients with a uniquely minimally invasive treatment option to whiten teeth. Since 1989, when Haywood and Heymann published the first article documenting the technique of 'nightguard vital bleaching',[2] much research has been undertaken to document its safety and effectiveness.[3]

On the 31 October 2012, the EU Council Directive 2011/84/EU came into force.[4] This stated that 'Tooth whitening or bleaching

products [containing concentrations] greater than 0.1 % or less than 6 % of H2O2 (Hydrogen peroxide), present or released [are] to be only sold to dental practitioners.' Use of 0.1% HP is much lower in concentration than that recommended for vital tooth bleaching, which commonly involves the use of 10–16% CP (10% carbamide peroxide breaks down into urea and 3.34% hydrogen peroxide).

As a result of directive 2011/84/EU, there has been an increase of 'non-hydrogen peroxide' products that have entered the market, to be purchased over the counter. These products contain a range of active ingredients, with limited research on their safety and efficacy. Many OTC products are in the form of whitening dentifrices; however, these will not be discussed

Table 1 Product names, manufacturers, ingredients and active ingredients				
Group	Product	Manufacturer	Ingredients	Active ingredient
Number 1	PolaNight	SDI (Bayswater, Australia)	Glycerin, aqua, PEG12, carbamide peroxide (10%), carbomer, sodium hydroxide, aroma, sodium fluoride	10% carbamide peroxide
Number 2	Distilled water	N/A	Distilled water	Distilled water
Number 3	Brilliant 5 minute kit	Lornamead (Harrison, USA)	Accelerator: aqua, sodium chlorite. Whitening gel ingredients: aqua, carbomer, glycerin, pollysorbate 20, PVP, sodium hydroxide, citric acid, mentha piperita (peppermint oil) pentasodium triphosphate, methylparaben, limonene	Sodium chlorite
Number 4	Smile Science Harley Street professional teeth whitening kit	Smile Science (Westfield, UK)	Glycerin, aqua, menthe piperita oil, carbomer, triethanolamine, mica, sodium carbonate peroxide, sucralose, linalool, Dlimonine	Sodium carbonate peroxide
Number 5	iWhite instant teeth whitening	Sylphar NV (Belgium, Deurle)	Aqua, hydrated silica, glycerin, sorbitol, chondrus crispus powder PEG40 hydrogenated castor oil, phthalimidoperoxycaproic acid, aroma, citric acid, methylparaben, acrylates/acrylamide copolymer, paraffinum liquidum, xylitol, calcium gluconate, potassium acesulphame, polysorbate 85, BHT	Phthalimidoperoxycaproic acid (PAP)
Number 6	Mr Blanc Teeth	Mr Blanc Teeth Ltd (Leeds, UK)	Glycerin, aqua, cellulose gum, sodium chlorite, EDTA, citric acid, D. L menthol	Sodium chlorite
Number 7	Janina Ultra White	Brodie and Stone (London, UK)	Glycerin, aqua, cellulose gum, sodium chlorite, EDTA, menthol, citric acid	Sodium chlorite

in this study and have been covered elsewhere.[5] The lack of research and ease of availability of these products from major consumer outlets is alarming, as it may potentially be harming the consumers' dentition. Further concerns with over the counter products are the risk of misuse, overuse and abuse because of their 'DIY' nature.[6] The aim of this study was to determine whether new non-hydrogen peroxide OTC products available in the UK are safe, by analysing changes in microhardness and by analysing changes to enamel surface in scanning electron microscopy. Furthermore, the lightening effect of the OTC agents was evaluated.

Materials and methods

Five over the counter whitening products from two major consumer outlets, Boots and Superdrug, were selected. A positive control of 'PolaNight' (10% carbamide peroxide was used) and a negative control of saline. The different products used are listed in Table 1.

Twenty-one freshly extracted teeth (11 incisors and ten bicuspids) were collected and stored in water with 1% chloramine-T (chlT) for three months before the study. Five days before the study, all teeth were immersed in 5 ml of a standard green tea solution in a beaker at room temperature (22±2 °C) to produce stained samples. The tea solution was produced by boiling 5.6 g of tea in 400 ml of distilled water for five minutes and filtered through gauze to remove the tea from the infusion. Some may argue that the use of tea solution is insufficient to

induce a discolouration similar to that observed in natural intrinsic discolouration. However, a study by Sulieman et al.[7] (2003) demonstrated that tea reliably produced an intrinsic stain consistent with tooth discolouration observed clinically and assessed by shade guide systems employed clinically. Furthermore, such protocol forms standard method for measuring the bleaching effect in vitro.[8,9,10]

The roots of the teeth were sectioned from the crowns. The teeth were then cleaned using an ultrasonic bath, to remove any sources of blood or debris from the surface of the tooth and the majority of extrinsic surface staining. The teeth were embedded in cold cure resin (Plexcil C6, Escil, Chassieu, France). The buccal aspects of the teeth were flattened using a series of high abrasive discs (800- 4,000 grids) and stored overnight in a tea solution.

The initial shade of the teeth was determined blindly by a single trained clinician using a Vita 3D Master shade guide in a natural light environment against a grey background. The samples were sectioned longitudinally (inciso-gingivally) from the buccal aspect by a cooled, low-speed diamond IsoMet saw to serve as a paired test specimen. One incisor and one premolar were allocated to each of the seven groups from Table 1, with the remaining samples randomly allocated to the seven groups. Three separate baseline Vickers microhardness values were recorded and SEM analysis of the control samples was undertaken.

Products were applied with a minimal thickness of 2–3 mm according to the

manufacturer's instructions for application (group four required LED light application, and groups six and seven were provided with polyether strips). Initially, products were applied to the teeth samples for two one-hour cycles. This was done to represent the abuse and misuse of products commonly associated with 'DIY' over the counter products.

Following this, the products were applied according to manufacturer's instructions to complete a seven-day cycle, as seen in Table 2. The samples were stored overnight in saline to minimise the effects that dehydration may have had. Shades of the control samples and experimental sample were retaken. Three Vickers microhardness values were taken on each paired test specimen (three on the control section, three on the section undertaking treatment). Teeth were then prepared for SEM analysis, which was undertaken on all samples.

Statistical analysis

The Vickers microhardness of the experimental and control halves were statistically compared to the baseline values using Wilcoxon tests (p <0.05). Statistical analysis was performed using IBM SPSS version 23. Shade changes were analysed quantitatively by assigning each shade tab of the 3D Master shade guide a number based on the value of the shade (1–26). A positive numerical change indicated that the tooth was getting lighter. The sum of shade changes was totalled for all samples, and products were ranked based on the total increase in shade (Table 3).

Results

The SEM analysis of the samples revealed enamel surface morphology alterations following application of non-peroxide OTC products. The greatest alterations were those in group three (Fig. 1) and group five (Fig. 2), which resulted in dissolution of enamel surface, exposing enamel crystallites and produced a distinct etching pattern across the surface of samples, similar to that observed with phosphoric acid. Products in groups four, six and seven also resulted in morphological alterations of enamel surface, including surface erosion and pitting, enamel surface dissolution and etching patterns less extensive than those in groups three and five.

The negative control used in group two resulted in no morphological alteration in SEM analysis. The positive control used in group one produced few to mild surface alterations with some surface depressions noted. Importantly, such alterations were noticeably less than those present in groups three, four, five, six and seven.

Vickers microhardness results (Table 4) revealed that two of the products, product three ('Brilliant 5 minute kit', p = 0.008), and product five ('iWhite', p = 0.008), produced significant reductions of the samples microhardness (P <0.05). All products other than saline (product one) and 'Smile science professional white' (product four) resulted in a mean reduction in Vickers microhardness.

All products resulted in a lightening effect, however two of the products resulted in less change than the negative control of saline. Furthermore, two of the products resulted in a greater cumulative change than that of the positive control of carbamide peroxide.

Discussion

The aim of this study was to evaluate the effectiveness and safety of over the counter whitening products available in the UK. Traditionally, whitening products used by dentists in the UK contain either 6% hydrogen peroxide or 10% carbamide peroxide (which breaks down into urea and 3.34% hydrogen peroxide). Research into the safety of these products has demonstrated no significant alteration in microhardness and mineral content, and most SEM studies show little or no changes of bleached enamel surface.[11,12,13,14,15,16,17,18,19] Significant bleaching effects have been demonstrated with the peroxide products in *in situ* clinical studies.[20,21,22,23,24,25] Furthermore,
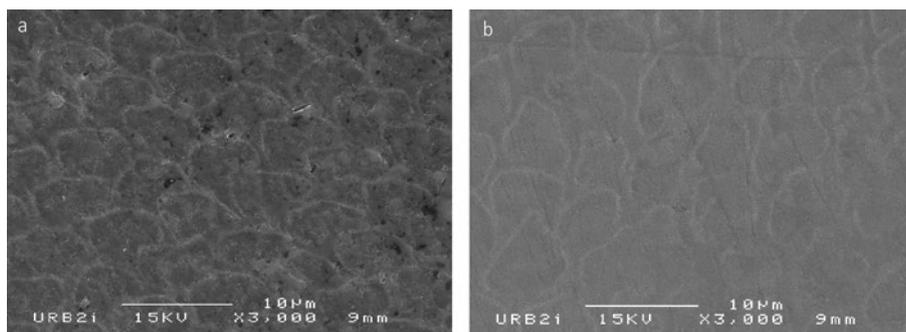

Fig. 1 Typical micrographs of samples post-application of group three product. A distinct etching pattern across the surface of the enamel can be observed
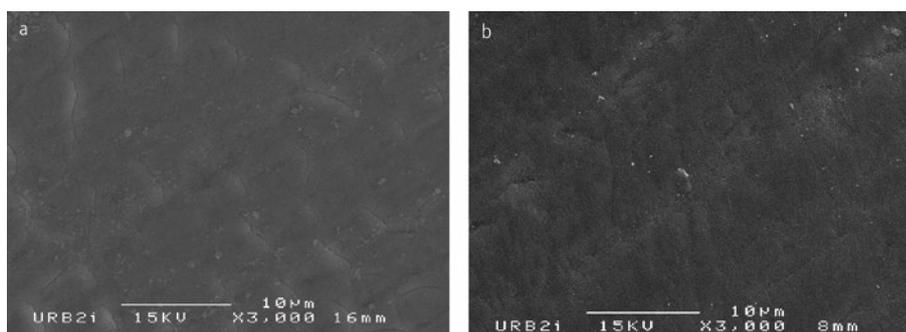

Fig. 2 Typical micrographs of samples post-application of group five OTC bleaching product. A distinct pattern shown across the surface of samples can be observed

Table 2 Details of the instruction of use for the products and the cycles use to apply product to each sample

Group	Instructions for use	Details of cycles applied to sample
Number 1	1 hour each day	2 x 1 hour cycles, additional 5 x 1 hour cycles
Number 2	1 hour each day	2 x 1 hour cycles, additional 5 x 1 hour cycles
Number 3	2 x 5 mins cycles for each day use	2 x 1 hour cycles, additional 12 x 5 min cycles
Number 4	1 x 20 mins cycle daily	2 x 1 hour cycles, additional 5 x 20 min cycles
Number 5	1 x 20 mins cycle daily	2 x 1 hour cycles, additional 5 x 20 min cycles
Number 6	1 x 30 min cycle daily	2 x 1 hour cycles, additional 5 x 30 min cycles
Number 7	2 x 30 mins cycles daily	2 x 1 hour cycles, additional 12 x 30 min cycles

urea from the degradation of CP has also been shown to be antibacterial in nature,[26,27] and to elevate salivary flow rates and salivary pH,[28] thus resulting in an anti-cariogenic effect. CP has also been shown to result in a reduction in bleeding on probing, plaque index and gingival index scores.[29,30]

The research into non-peroxide OTC products is minimal.[31] The active ingredient in three of the OTC products was sodium chlorite (SC). Sodium chlorite liberates a small amount of chlorine dioxide (ClO_2) in the presence of acid.[32] Initial studies into products containing SC and ClO_2 have suggested that these products reduce the microhardness of enamel. Additionally, as a result of an extensively long period of re-hardening following application of SC and ClO_2 bleaching products, there is an increased susceptibility to surface abrasion.[32] A study by Alabal *et al.*[33] examining the whitening effect of chlorine dioxide and the pH of the product, found that chlorine dioxide whitens teeth at a faster rate than hydrogen peroxide; however, it resulted in a significantly lower pH in comparison to hydrogen peroxide and as such should not be used.

Besides sodium chlorite, the European ban on peroxide containing whitening products has resulted in other alternative active ingredients being produced. Product four has an active ingredient of sodium carbonate peroxide, while product five contained phthalimidoperoxycaproic acid (PAP). Sodium carbonate peroxide, also known as sodium percarbonate $(2Na_2CO_3.3H_2O_2)$, releases hydrogen peroxide on breakdown and as such further studies are required to demonstrate the quantity of hydrogen peroxide released, and if such products comply with EU Council Directive 2011/84/EU.

Furthermore, besides product four, all the OTC products contained citric acid (CA). It is believed that the citric acid is used in these products as an accelerator.[33] None of the control products examined in the study contained CA. Citric acid is the main acid in many fruit drinks and juices, and has been shown to have an erosive nature,[34] with many *in vitro* investigations demonstrating enamel dissolution in citric acid solutions.[35,36,37,38] However, an *in vitro* study by Eisenburger *et al.*[39] suggests that a complete re-hardening of citric acid softened enamel is reached after a remineralisation time of six hours. Furthermore, a more recent *in vitro* study by Ionta *et al.*[40] also demonstrated this re-hardening effect post-exposure to artificial saliva. Therefore, further research on the OTC products without citric acid, and post six hours of exposure to artificial saliva, would be beneficial.

Newer CP and HP products have introduced sodium fluoride (SF) and potassium nitrate (PN) into their products to promote remineralisation and reduce sensitivity. A split-mouth study by Tam *et al.*[41] demonstrated that the addition of PF and SF to 10% carbamide peroxide resulted in a significant reduction in sensitivity experienced by patients. However, none of the OTC products contained SF or PN. As the OTC products were tested *in vitro*, the effect of the OTC products on sensitivity could not be measured. However, it is the authors' opinion that the OTC products would result in increased sensitivity episodes, due to the products containing erosive elements, such as citric acid, and lacking elements which help reduce sensitivity, such as SF and PN. Furthermore, SEM micrograph results demonstrated dissolution of enamel surface and interprismatic enamel, following application of the OTC products, and therefore an increased tendency to underlying dentine exposure.

Table 3 Shade change between control and treatment, using the Vita 3D Master shade guide

Product shade ranking (most to least)	Cumulative shade change	Shade pre-treatment	Shade post-treatment
Group 6: Mr Blanc teeth strips	+35	5m3 4m3 3l2.5	3m2 2m2 2l2.5
Group 7: Janina strips	+30	4m3 3m3 4m2	2l2.5 2m2 3m3
Group 1: PolaNight 10%carbamide peroxide	+26	3m2 4l2.5 4r1.5	2l1.5 2r1.5 3r2.5
Group 3: Brilliant 5 minute kit	+20	3m3 5m3 3r1.5	2m2 3m2 3r1.5
Group 2: Saline	+7	4m3 3m3 5m3	4m2 3r2.5 5m3
Group 5: iWhite	+3	4l2.5 4m3 4m2	2m3 4r 1.5 4m2
Group 4: Smile professional science	+1	3l2.5 4m3 4m2	3m2 4r2.5 4m2

Table 4 Vickers microhardness values of control and treatment samples

Group	Product	Mean Vickers microhardness control	Mean Vickers microhardness treatment	P-value (P<0.05)
1	PolaNight (10% carbamide peroxide)	328.52 (±29.52)	314.58 (±27.51)	0.173
2	Saline	280.91 (±27.77)	285.13 (±49.35)	0.594
3	Brilliant 5 minute kit	301.26 (±25.37)	276.289 (±23.58)	*0.008
4	Smile Science professional white	298.32 (±29.73)	304.37 (±23.19)	0.678
5	iWhite	323.33 (35.78)	300.00 (±26.89)	*0.008
6	Mr Blanc teeth strips	305.19 (±14.11)	301.60 (±16.97)	0.859
7	JANINA	305.48 (±16.38)	293.81 (±21.32)	0.374
*significance at 5%				

All products, except products two and four, resulted in reductions in Vickers microhardness. However, only products three and five resulted in significant reductions. These two products were also associated with the greatest surface alterations observed in SEM analysis. These products contained different active ingredients, however, both contained citric acid. The SEM results for both products were similar, producing etching effects on the enamel surface and a loss of interprismatic enamel. This may suggest that the citric acid in the product might result in the surface alterations, rather than the active ingredient itself. Carbamide peroxide (product one) also resulted in reductions in Vickers microhardness, however, this was not significant and has been repeatedly demonstrated to be not significant in both in vitro and in vivo studies.[11,12,13,14,15,16,17,18,19] This is thought to result from its effect on elevating saliva and plaque pH.[27]

Product five ('iWhite') resulted in a lightening effect less than that of the negative control saline. The lack of lightening effect is of concern, as this may result in consumers overusing the product in an attempt to produce a satisfactory lightening change, also known as a 'catch-up' mentality. This may result in greater damage to enamel, especially when combined with the acidic nature of the active ingredient, phthalimidoperoxycaproic acid.

However, further research on the ingredient's is still required.

The group three product ('Brilliant 5 minute smile') produced a lightening effect less than CP, but greater than that of the negative control, saline. SEM analysis of product three revealed the greatest damage to enamel surface of all products. Therefore, it would be plausible that the lightening effect observed may result from changes to the optical properties of the enamel surface of the samples, somewhat similar to the 'frosty appearance' observed post-application of acid etch. Although not completely understood, it is generally accepted that peroxide-based bleaching agents produce a lightening effect by producing free radicals, while diffusing through enamel and dentine, breaking double bonds of pigment molecules and changing the pigment molecule configuration and/or size.[3]

Surprisingly, two of the OTC products, product six ('Mr Blanc') and product seven ('Janina') produced a greater lightening effect than the positive control (CP). These products were the only polyethene strip associated products and were the only products applied with a carrier. The polyethene strips may have resulted in greater surface contact between the products and the enamel, resulting in an increased effect. As no other products were applied with a carrier, this would present a limitation of the study. Randomised clinical trials on 5.3–6% HP polyethene strips in comparison to tray-applied 10–20% CP have noted either no statistical difference or an improvement in lightening effect favouring the polyethene group.[42,43] Limitations of polyethene strip systems include adaption to malocclusion and mandibular retention.[44]

Sodium chlorite was the active ingredient in three of the four products which produced the greatest lightening effect, with the other being CP. Although this would suggest SC is inducing a bleaching effect, there are several limitations which prevent this being definitively concluded. Firstly, as mentioned previously, SC-induced enamel surface changes may explain the lightening effect observed. There are several issues associated with this type of whitening. Rough enamel surfaces have been shown to result in increased plaque accumulation[45,46] due to rough enamel having a higher surface energy. This would result in increased susceptibility to gingivitis and periodontitis. Furthermore, increased surface roughness and surface energy may also result in increased stain accumulation.[47]

Another limitation of this study, which prevents a definitive conclusion of SC's bleaching effect, is that only the enamel surface could be measured for shade change. It could be distinctly possible that the lightening effect associated with SC products results from optical changes to enamel surface only, with little effect to the inner enamel or dentine. Whitening effects limited to superficial enamel surfaces increased the likeliness of relapse, due to a failure to reach the bleaching potential. Ultimately, further research would be required to definitively categorise SC's bleaching effect. A study similar to McCaslin *et al.*[48] would be beneficial to measure the bleaching effect of the OTC products on the inner enamel and dentine layers.

As mentioned previously, one of the well-known issues associated with OTC products is the potential for their misuse and abuse.[5] As the products are purchased without prior dental professional consultation, pre-operative instructions are limited. Therefore, no emphasis on following product instructions can be emphasised, and ultimately it is left to patient discretion and reading of product instructions to ensure correct product use. This has been shown to be ineffective throughout the medical and dental fields.[49] As such, incorporating this issue into study design was key to ensure a realistic representation of product effect and complete safety. Some may argue that such protocol may purposely exaggerate the etching effect of the acid containing products. It would, therefore, be beneficial to carry out additional research to compare the effect of misuse and non-misuse of OTC products. Other limitations of this in vitro study include the relatively small sample size and variation in the carrier type use for the product application.

Conclusion

Due to investigations in this pilot study, we concluded that OTC whitening products have the potential to reduce the hardness of enamel, induce surface alterations of enamel, and produce a lightening effect. However, further research remains for non-peroxide OTC whitening products. These include:

1. Considering the effect of concentration of both active ingredients and citric acid on enamel. It would be especially prudent to look at the effect of OTC products not containing citric acid

2. Determining if lightening effect is restricted to the enamel surface or takes place throughout enamel and dentine

3. Determining lightening effect *in vivo*

4. Determining effect of products on the oral environment, especially salivary pH and oral biofilm

5. Determining the effect of acidic dietary habits in combination with using OTC bleaching products

6. Determining the effect of OTC bleaching products on composite restorations, especially in the aesthetic zone

7. Determining the pH of the products.

This study also raises questions regarding EU Council Directive 2011/84/EU. Banning over-the-counter use of peroxide whitening products, although necessary, may not completely protect the public. As demonstrated by this study, there is a potential flaw in the system; allowing products with questionable safety and efficacy to be readily available to the public. The long-term effect of this, from a financial, psychological and dental standpoint is still in question.

References

1. National Institute of Teeth Whitening. Teeth Whitening Industry's Annual Revenue in 2015 Totals $11 Billion. 2015.
2. Haywood V B, Heymann H O. Nightguard vital bleaching. *Quintessence Int* 1989; **20:** 173–176.
3. Li Y, Greenwall L. Safety issues of tooth whitening using peroxide-based materials. *Br Dent J* 2013; **215:** 29–34.
4. European Union. EU Council Directive 2011/84/EU of 20 September 2011. Available at https://eur-lex.europa.eu/riServ/LexUriServ.do?uri=OJ:L:2011:283:0036:0038:en:PDF (accessed January 2019).
5. Joiner A. Whitening toothpastes: a review of the literature. *J Dent* 2010; **38:** e17–e24.
6. Kwon S R, Meharry M, Oyoyo U, Li Y. Efficacy of doityourself whitening as compared to conventional tooth whitening modalities: an in vitro study. *Oper Dent* 2015; **40:** E21–E27.
7. Sulieman M, Addy M, Rees J S. Development and evaluation of a method in vitro to study the effectiveness of tooth bleaching. *J Dent* 2003; **31:** 415–422.
8. Soares D G, Basso F G, Pontes E C, da F R Garcia L, Hebling J, de Souza Costa C A. Effective tooth-bleaching protocols capable of reducing H2O2 diffusion through enamel and dentine. *J Dent* 2014; **42:** 351–358.
9. Polydorou O, Hellwig E, Hahn P. The efficacy of three different in-office bleaching systems and their effect on enamel microhardness. *Oper Dent* 2008; **33:** 579–586.
10. Ristic I, Stankovic S, Paravina R D. Influence of color education and training on shade matching skills. *J Esthet Restor Dent* 2016; **28:** 287–294.
11. Haywood V B, Leonard R H, Dickinson G L. Efficacy of six-months nightguard vital bleaching of tetracycline-stained teeth. *J Esthet Dent* 1997; **9:** 13–19.
12. Bitter N C. A scanning electron microscope study of the long-term effect of bleaching agents on the enamel surface in vivo. *Gen Dent* 1998; **46:** 84–88.
13. Potocnik I, Kosec L, Gaspersic D. Effect of 10% carbamide peroxide bleaching gel on enamel microhardness, microstructure, and mineral content. *J Endod* 2000; **26:** 203–206.
14. White D J, Kozak K M, Zoladz J R, Duschner H, Götz H. Peroxide interactions with hard tissues: effects on surface hardness and surface/subsurface ultrastructural properties. *Compend Contin Educ Dent* 2002; **23:** 42–48.
15. Lopes G C, Bonissoni L, Baratieri L N, Vieira L C, Monteiro S Jr. Effect of bleaching agents on the hardness and morphology of enamel. *J Esthet Restor Dent* 2002; **14:** 24–30.

16. Attin T, Schmidlin P R, Wegehaupt F, Wiegand A. Influence of study design on the impact of bleaching agents on dental enamel microhardness: a review. *Dent Mater* 2009; **25:** 143–157.

17. Berger S B, Cavalli V, Martin A A *et al.* Effects of combined use of light irradiation and 35% hydrogen peroxide for dental bleaching on human enamel mineral content. *Photomed Laser Surg* 2010; **28:** 533–538.

18. Li Q, Xu B T, Li R, Yu H, Wang Y N. Quantitative evaluation of colour regression and mineral content change of bleached teeth. *J Dent* 2010; **38:** 253–260.

19. Justino L M, Tames D R, Demarco F F. In situ and in vitro effects of bleaching with carbamide peroxide on human enamel. *Oper Dent* 2004; **29:** 219–225.

20. Sun L, Liang S, Sa Y *et al.* Surface alteration of human tooth enamel subjected to acidic and neutral 30% hydrogen peroxide. *J Dent* 2011; **39:** 686–692.

21. Mokhlis G R, Matis B A, Cochran M A, Eckert G J. A clinical evaluation of carbamide peroxide and hydrogen peroxide whitening agents during daytime use. *J Am Dent Assoc* 2000; **131:** 1269–1277.

22. Leonard R H Jr, Bentley C, Eagle J C, Garland G E, Knight M C, Phillips C. Nightguard vital bleaching: a long-term study on efficacy, shade retention, side effects, and patients' perceptions. *J Esthet Restor Dent* 2001; **13:** 357–369.

23. Matis B A, Mousa H N, Cochran M A, Eckert G J. Clinical evaluation of bleaching agents of different concentrations. *Quintessence Int* 2000; **31:** 303–310.

24. Matis B A, Cochran M A, Eckert G, Carlson T J. The efficacy and safety of a 10% carbamide peroxide bleaching gel. *Quintessence Int* 1998; **29:** 555–563.

25. Al Shethri S, Matis B A, Cochran M A, Zekonis R, Stropes M. A clinical evaluation of two in-office bleaching products. *Oper Dent* 2003; **28:** 488–495.

26. Bentley C D, Leonard R H, Crawford J J. Effect of whitening agents containing carbamide peroxide on cariogenic bacteria. *J Esthet Dent* 2000; **12:** 33–37.

27. Yao C S, Waterfield J D, Shen Y, Haapasalo M, MacEntee M I. In vitro antibacterial effect of carbamide peroxide on oral biolfilm. *J Oral Microbiol* 2013; **5:** DOI: 10.3402/jom.v5i0.20392.

28. Leonard R H Jr, Bentley C D, Van Haywood B. Salivary pH changes during 10% carbamide peroxide bleaching. *Quintessence Int* 1994; **25:** 547–550.

29. Almas K, Al-Harbi M, Al-Gunaim M. The effect of a 10 percent carbamide peroxide home bleaching system on the gingival health. *J Contemp Dent Pract* 2003; **4:** 32–41.

30. Brunton P A, Ellwood R, Davies R. A six-month study of two self-applied tooth whitening products containing carbamide peroxide. *Oper Dent* 2004; **29:** 623–626.

31. Greenwall L. The dangers of chlorine dioxide tooth bleaching. *Aesth Dent Today* 2008; **2:** 21–23.

32. Zantner C, Beheim-Schwarzbach N, Neumann K, Kielbassa A M. Surface microhardness of enamel after different home bleaching procedures. *Dent Mater* 2007; **23:** 243–250.

33. Ablal M A, Adeyemi A A, Jarad F D. The whitening effect of chlorine dioxide: an in vitro study. *J Dent* 2013; **41 (Spec Iss):** e76–e81.

34. Lussi A, Jaeggi T, Jaeggi-Schärer S. Prediction of the erosive potential of some beverages. *Caries Res* 1995; **29:** 349–354.

35. West N X, Hughes J A, Addy M. The effect of pH on the erosion of dentine and enamel by dietary acids in vitro. *J Oral Rehab* 2001; **28:** 860–864.

36. Hughes J A, West N X, Parker D M, van den Braak M H, Addy M. Effects of pH and concentration of citric, malic and lactic acids on enamel, in vitro. *J Dent* 2000; **28:** 147–152.

37. Eisenburger M, Addy M. Evaluation of pH and erosion time on demineralisation. *Clin Oral Investig* 2001; **5:** 108–111.

38. Barbour M E, Parker D M, Jandt K D. Enamel dissolution as a function of solution degree of saturation with respect to hydroxyapatite: a nanoindentation study. *J Colloid Interface Sci* 2003; **265:** 9–14.

39. Eisenburger M, Addy M, Hughes J A, Shellis R P. Effect of time on the remineralisation of enamel by synthetic saliva after citric acid erosion. *Caries Res* 2001; **35:** 211–215.

40. Ionta F Q, Mendonça F L, de Oliveira G C *et al.* In vitro assessment of artificial saliva formulations on initial enamel erosion remineralization. *J Dent* 2014; **42:** 175–179.

41. Tam L. Effect of potassium nitrate and fluoride on carbamide peroxide bleaching. *Quintessence Int* 2001; **32:** 766–770.

42. Gerlach R W, Gibb R D, Sagel P A. A randomized clinical trial comparing a novel 5.3% hydrogen peroxide whitening strip to 10%, 15%, and 20% carbamide peroxide tray-based bleaching systems. *Compend Contin Educ Dent Suppl* 2000; **29 (Spec Iss):** S22–S28.

43. Ferrari M, Cagidiaco M C, Monticelli F, Kugel G, Barker M L, Gerlach R W. Daytime use of a custom bleaching tray or whitening strips: initial and sustained colour improvement. *Am J Dent* 2007; **20 (Spec Iss):** 19A–22A.

44. Greenwall L H (ed). *Tooth whitening techniques.* 2nd ed. London: Taylor and Francis, 2017.

45. Hosoya N, Honda K, Iino F, Arai T. Changes in enamel surface roughness and adhesion of Streptococcus mutans to enamel after vital bleaching. *J Dent* 2003; **31:** 543–548.

46. Quirynen M, Bollen C M. The influence of surface roughness and surface-free energy on supra-and subgingival plaque formation in man. A review of the literature. *J Clin Periodontol* 1995; **22:** 1–14.

47. Cavalli V, Arrais C A, Giannini M, Ambrosano G M. High-concentrated carbamide peroxide bleaching agents effects on enamel surface. *J Oral Rehabil* 2004; **31:** 155–159.

48. Mccaslin A J, Haywood V B, Potter B J, Dickinson G L, Russell C M. Assessing dentin colour changes from nightguard vital bleaching. *J Am Dent Assoc* 1999; **130:** 1485–1490.

49. Frei M Y, Nielsen S, Dobbin M D, Tobin C L. Serious morbidity associated with misuse of overthecounter codeine-ibuprofen analgesics: a series of 27 cases. *Med J Aust* 2010; **193:** 294–296.