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ORIGINAL ARTICLE

A new three-component formulation for the efficient whitening of teeth (Carbamide Plus)

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Abstract
Objectives This study aimed to develop and characterise a new three-component dental whitening formulation which is as effective as the currently used carbamide peroxide but at significantly lower hydrogen peroxide concentrations.
Materials and methods The new formulation (Carbamide Plus) was prepared containing hydrogen peroxide, urea, and sodium tripolyphosphate and compared directly with carbamide peroxide (containing just hydrogen peroxide and urea). To evaluate the clinical effectiveness of 5 % Carbamide Plus, a randomised double-blind placebo-controlled clinical trial was conducted comparing the tooth colour of 33 patients using $L^*a^*b^*$ scores at baseline and after a 2-week whitening treatment. The behaviour of the three components in solution was determined by ^{1}H and ^{31}P NMR spectroscopy and pH dilution experiments.
Results This clinical trial revealed that 5 % whitening gels containing Carbamide Plus were as effective as those containing 10 % carbamide peroxide. ^{1}H and ^{31}P NMR spectroscopy revealed strong intermolecular interactions between hydrogen peroxide and both urea and sodium tripolyphosphate (STPP) with little apparent interaction between urea and STPP.
Conclusions In this manuscript, we postulate that this increased whitening efficiency is due to a marked increase in local pH upon dilution which destabilises the hydrogen peroxide and expedites the whitening process. We postulate Carbamide Plus to be a three-component adduct with two molecules of carbamide peroxide binding to a central STPP unit with no direct interaction between STPP and urea. There were no statistically significant differences between Carbamide Plus and 10 % carbamide peroxide in tooth-whitening achieved at 2 weeks. These results were recorded following 2 weeks of 2-h daily wear of at-home trays.
Clinical relevance Carbamide Plus offers the potential of using significantly lower levels of hydrogen peroxide concentration to achieve similar dental whitening effects.

Keywords STPP · Hydrogen peroxide · NMR spectroscopy · pH · Carbamide peroxide · Carbamide Plus

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Introduction

In 1989, Haywood and Heymann introduced the first 'Night-Guard Vital Bleaching" technique where a 10 % carbamide peroxide gel formulation was applied to the teeth overnight using a customised tray [1]. Although there are many variations of both the technique and the whitening agent used, the fundamentals of applying a hydrogen peroxide (HP)-containing gel to teeth remain [2]. In the past, dentists advised that the mouth tray and whitening agent be worn overnight to achieve maximum results [3, 4]. However, it has been shown that the active ingredient hydrogen peroxide degrades exponentially over time [5]. As a result, it has been suggested to use the whitening trays for only 2 to 4 h/day [6] thus potentially decreasing the occurrence and severity of the common side effects gingival irritation and tooth sensitivity [7–9]. Carbamide peroxide is a 1:1 adduct of hydrogen peroxide and urea

[10] and is the most commonly used whitening agent for teeth. In aqueous solutions, it readily dissociates to give urea and hydrogen peroxide [11], the latter being an effective oxidising agent [12]. Hydrogen peroxide can further dissociate to give reactive oxygen species (ROS), and it is these species that are thought to be responsible for intrinsic dental stain removal [13]. The most reactive of these ROS is the perhydroxyl ion which is optimally released in an alkaline environment (pH of around 10) [14]. However, these conditions are rarely encountered since most home-use commercial whitening products have a pH of around 6.5 to ensure a longer shelf life [13]. Some products have a pH as low as 5 and concern has been raised about their possible erosive effect [15]. Since hydrogen peroxide is a weak acid, it is most stable in acidic conditions and its dissociation is favoured by alkaline conditions. The urea present in carbamide peroxide can also decompose into ammonia and carbon dioxide [12, 16, 17] which elevates the pH, thus facilitating the whitening process. It has previously been demonstrated that raising the pH to alkaline conditions during peroxide whitening results in a significantly increased tooth whiteness when compared to hydrogen peroxide at its normal pH of 4.4 [18]. The elevated pH lowers the activation energy required to form hydrogen peroxide-based free radicals [12]. Therefore, it is clear that pH plays a vital role in the efficiency of dental whitening formulations.

Our interest in this area has led us to hypothesise that if the local pH environment of hydrogen peroxide could be increased upon application of the whitening gel, then this should catalyse the decomposition of hydrogen peroxide and expedite the whitening process. Prolonged exposure to high concentrations of hydrogen peroxide can result in significant tooth sensitivity and gingival irritation [19, 20]. Therefore, the ability to achieve efficient whitening at lower levels of hydrogen peroxide over a shorter period of time has obvious benefits to the end user.

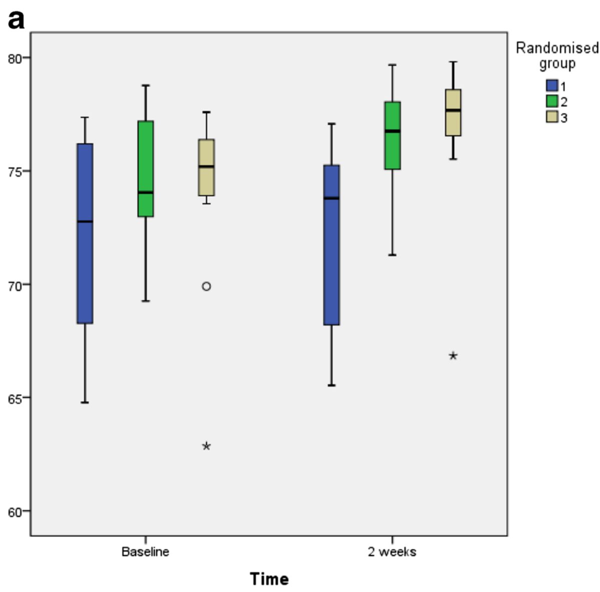
In this manuscript, we have developed a new three-component formulation for whitening teeth named Carbamide Plus. In addition to containing hydrogen peroxide and urea, this new formulation differs from carbamide peroxide in that it also contains sodium tripolyphosphate (STPP). STPP has previously been shown to form a complex with hydrogen peroxide [21], and as hydrogen peroxide is also known to form a complex with urea, we were interested to learn how these three components would interact when present together in solution and what effect this would have on whitening performance. Furthermore, STPP may have additional benefits when present in dental whitening formulations as it has previously been shown to be an effective agent for inhibiting and removing extrinsic dental staining [22, 23] as well as being an anti-calculus agent in both dentifrices [24, 25] and chewing gum [26, 27]. Here, we investigate the structure and properties of this new three-component formulation and determine its potential as a dental whitening agent in a randomised clinical trial.

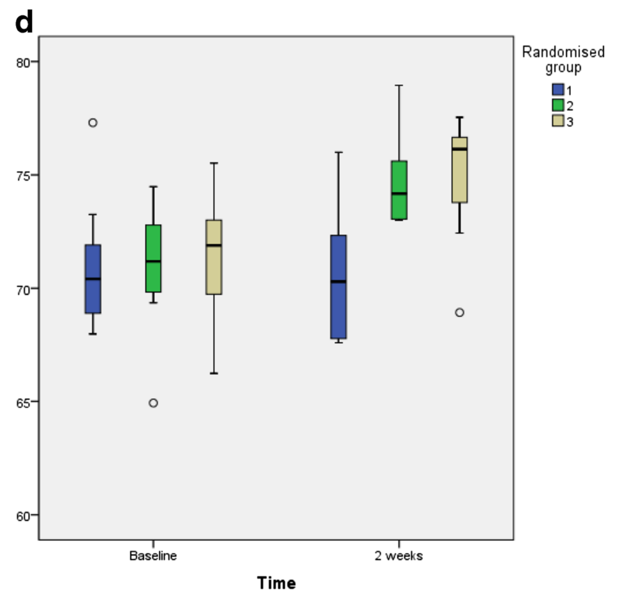
Fig. 1 **a** Boxplot graph of the 95 % confidence interval of the L^* values (UL1) of the three study groupings at baseline and 2 weeks. **b** Boxplot graph of the 95 % confidence interval of the a^* values (UL1) of the three study groupings at baseline and 2 weeks. **c** Boxplot graph of the 95 % confidence interval of the b^* values (UL1) of the three study groupings at baseline and 2 weeks. **d** Boxplot of L graph of the 95 % confidence interval of the L^* values (UR3) of the three study groupings at baseline and 2 weeks. **e** Boxplot graph of the 95 % confidence interval of the a^* values (UR3) of the three study groupings at baseline and 2 weeks. **f** Boxplot graph of the 95 % confidence interval of the b^* values (UR3) of the three study groupings at baseline and 2 weeks

Materials and methods

pH dilution analysis The three active components in Carbamide Plus gel are in the ratio of 19.21:15.42:65.37 (STPP/urea/35 % hydrogen peroxide, respectively). Initially, 50 % *w/v* solutions containing the three components were prepared by weighing out the relative amounts of each component (total weight of 2.0 g) into a beaker and dissolving in 2 ml of distilled water. The initial pH values of these solutions were recorded and then subsequently diluted by addition of distilled water by pipette to a final concentration of 5.0 % *w/v* with the pH recorded at each dilution interval. In order to directly compare pH upon dilution of each individual component to the dilution of the three components, the amount of each component weighed out in the individual dilution experiments was identical to the amount used in the 'combined' three-component experiment. STPP is a basic salt and the amount used in these experiments equated to 0.001 mol. When comparing Carbamide Plus to carbamide peroxide, the amount of carbamide peroxide standard (97 % Sigma-Aldrich) used reflected the same hydrogen peroxide content in the Carbamide Plus dilution experiment. All pH dilution experiments were carried out in triplicate using a VWR symphony pH meter at 25 °C.

NMR studies Stock solutions of STPP (>92 % food grade, Prayphos) urea (98+%, Sigma-Aldrich) and 35 % hydrogen peroxide (35 % Interox Aseptic Grade, Solvay) were prepared in deuterium oxide (99 %, Sigma-Aldrich). The required amount of each solution was then micro pipetted into scintillation vials and mixed before pipetting into NMR tubes. All ^{31}P and ^{1}H NMR analysis was carried out on a Varian 500-MHz spectrometer at 25 °C. The spectra were processed using Bruker Topspin software. To determine the stoichiometry of the interactions observed, the method of continuous variations was used [28, 29]. Here, 0.5 M stock solutions of host and guest were used to prepare a series of nine solutions going from 0.9_{Host}:0.1_{Guest} to $\rightarrow 0.1_{Host}$:0.9_{Guest}. The total


a
Randomised group
1
2
3
80
75
70
65
60
Baseline
2 weeks
Time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1
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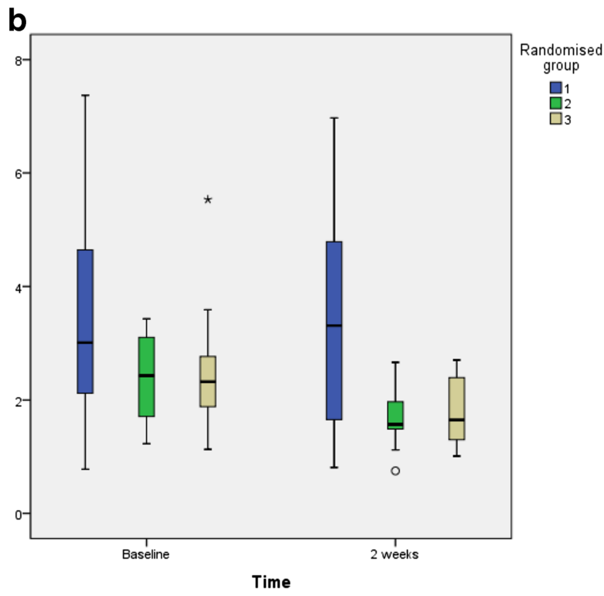
2 weeks
Time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3
8
6
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2
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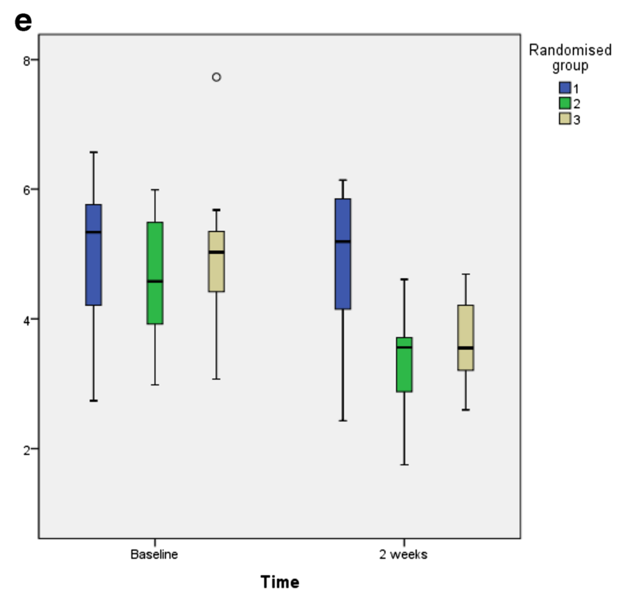
Baseline
2 weeks
Time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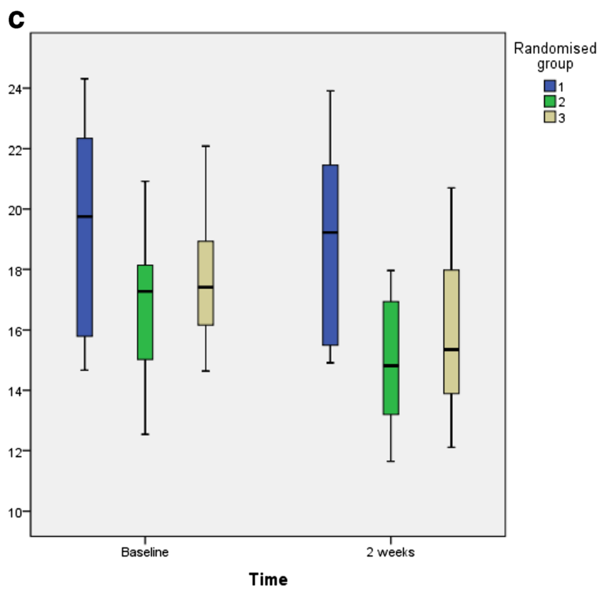
Baseline
2 weeks
Time


c
Randomised group
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24
22
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18
16
14
12
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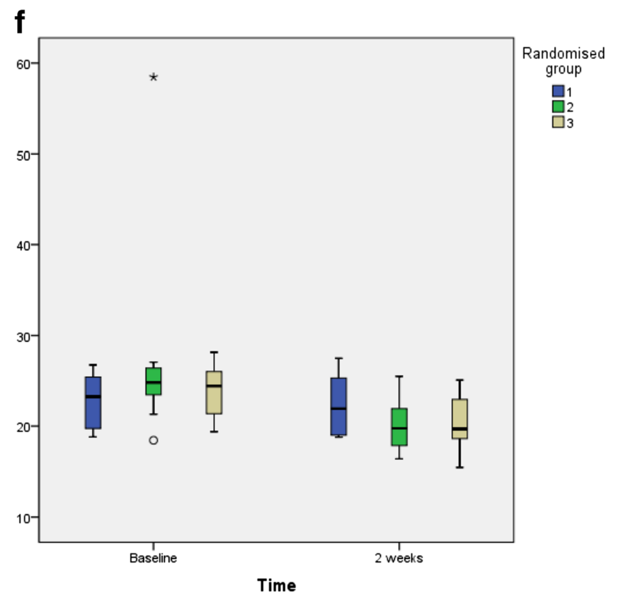
Baseline
2 weeks
Time


f
Randomised group
1
2
3
60
50
40
30
20
10
Baseline
2 weeks
Time

number of moles of host and guest remained constant. A Job's plot of (χ_H $\Delta\delta$) against mole fraction (χ_G) was plotted, where $\Delta\delta$ is the observed change in chemical shift of the host, χ_H is the mole fraction of the host, and χ_G is the mole fraction of the guest. The peak maxima of these plots were used to determine the stoichiometry of interactions.

Clinical trial Thirty-three subjects were recruited into this study from existing patients at the Eastman Dental Hospital. Exclusion criteria were heavily restored upper left central incisor or upper right canine, pregnancy or breastfeeding, patients who had previously undergone a course of vital tooth-whitening, smokers, active dental disease (caries and periodontal disease), severe dentine hypersensitivity, uncontrolled dental disease, and unable to attend on data collection days. The recruited subjects were randomly allocated to one of three study groupings: non-active placebo gel (group 1, n=11), 5 % Carbamide Plus gel (group 2, n=10), and a 10 % carbamide peroxide gel (group 3, n=11). Patients were seen at baseline (prior to commencement of tooth-whitening) and at 2 weeks (immediately upon completion of tooth-whitening). Application of the gels was performed using customised trays that were applied for 2 h/day over a 2-week period. The whitening effect of the gels was determined by measuring the colour of the upper left incisor (UL1) and upper right canine (UR3) using a SpectroShade spectrometer and the Commission Internationale de l'Eclairage (CIE) colour scale. $L^*a^*b^*$ parameters were measured. In CIE $L^*a^*b^*$, the L^* axis represents lightness ranging from 0 to 100, with 0 representing a perfect black and 100 a perfect reflector, a^* represents red-green, and b^* represents the blue-yellow component of the spectrum (b^*=yellowness of tooth). A Medical High Technologies (MHT) SpectroShade spectrophotometer was used to measure the tooth colour, and this was calibrated against green and white tiles before each colour measurement. A sterile mouthpiece was attached to the optical window for each patient. A digital viewing screen allowed the positioning of a horizontal green line across the mid-one third of the tooth crown. The SpectroShade then indicated if the recording was satisfactory and was then connected to a desktop PC and images uploaded to the MHT software. Patients were provided with a standardised non-tooth-whitening toothpaste (Colgate Total®) to use throughout the study period (Fig. 1).

Based on a two-sample t test with a significance level of 0.05 and a power of 80 %, it was necessary to recruit ten patients per group in order to detect a significance of a difference of at least 2.5 increase for lab values assuming a standard deviation of 1.2. To plan for possible loss to follow-up, it was decided to recruit 11 to each group. A two-way repeated measures hierarchical analysis of variance (ANOVA), a one-way ANOVA, and a post hoc Bonferroni tests were carried out. A significance level of 5 % was used throughout, and the data were analysed by SPSS (IBM Corp., Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.).

Results

Effect of dilution on pH of Carbamide Plus and carbamide peroxide To determine the effect of dilution on the pH of Carbamide Plus, a 50.0 % w/v solution in H_2O was prepared and subsequently diluted to a final concentration of 5.0 % w/v with the pH recorded at each dilution interval. This experiment was also repeated using carbamide peroxide under identical conditions. A plot of change in pH (ΔpH) against percent w/v for both Carbamide Plus and carbamide peroxide is shown in Fig. 2 and shows a significant increase in ΔpH for Carbamide Plus compared to carbamide peroxide. When this experiment was repeated with STPP alone, at the same concentration as it is present in Carbamide Plus, a significantly smaller pH increase (ΔpH=0.54) was observed upon dilution. This suggests the STPP interacts with the hydrogen peroxide and/or urea present in Carbamide Plus resulting in a different pH profile upon dilution. To probe this interaction further, we

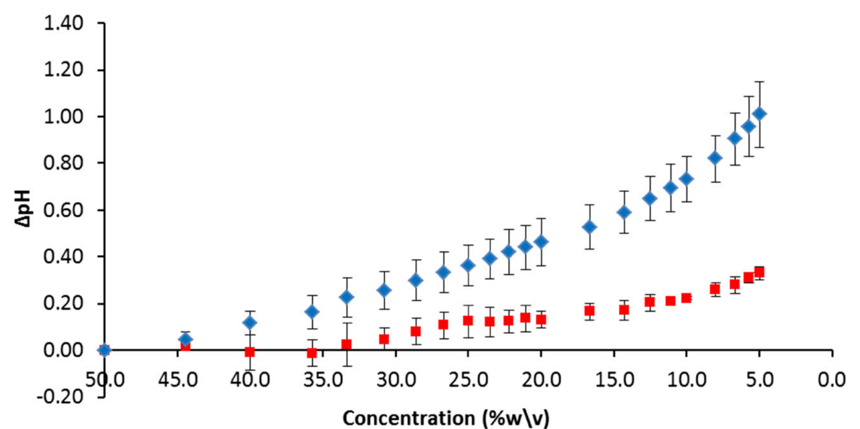


Fig. 2 Plot of ΔpH as a function of concentration for the three-component Carbamide Plus (*blue diamonds*) and carbamide peroxide (*red squares*). Error bars from the standard deviation are shown

also investigated the effect of dilution on hydrogen peroxide and urea independently. While the starting pH values for 50 % *w/v* solutions of hydrogen peroxide (pH=4.05) and urea (pH=9.44) are acidic and basic, respectively, both trend towards neutral pH upon dilution as expected. However, the magnitude of this change (i.e. ΔpH) was significantly greater for urea than for hydrogen peroxide. Therefore, to discount the possibility that the observed pH increase for Carbamide Plus upon dilution was not due to an 'additive' effect of each individual component, we combined the individual ΔpH values for STPP, hydrogen peroxide, and urea and plotted this as a function of percent *w/v*. As shown in Fig. 3, this plot reveals an overall reduction in pH upon increasing dilution which is contrary to that observed for Carbamide Plus. Collectively, these results suggest that when hydrogen peroxide, urea, and STPP are present together, they interact with each other in such a way that the solution becomes more basic as the water content is increased.

NMR studies To investigate this potential interaction further, we used NMR spectroscopy focussing on the ^{1}H nuclei of urea and the ^{31}P nuclei of STPP. Focussing on the ^{1}H nuclei of urea, we observed the broad singlet moves upfield upon increasing the amounts of hydrogen peroxide indicating a hydrogen bonding interaction between the two components (Fig. 4a). Using Jobs method of continuous variation, the binding stoichiometry was confirmed as 1:1 host/guest (Fig. 4b). A similar experiment was performed probing the interaction between hydrogen peroxide and STPP using ^{31}P NMR. An upfield shift in both the triplet at −19.4 ppm (representing the central phosphorus atom) and the doublet at −5.1 ppm (representing the two terminal phosphorus atoms) was observed upon increasing peroxide addition (Fig. 5a). The

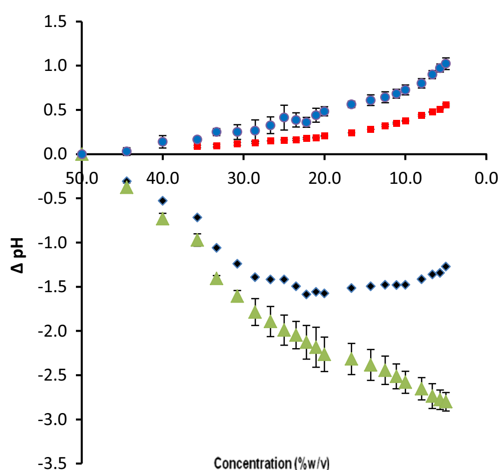


Fig. 3 Plot of ΔpH as a function of concentration for STPP alone (*red squares*), urea alone (*green triangles*), hydrogen peroxide alone (*blue circles*), and the combined addition of the ΔpH values for the three individual component curves (*black diamonds*). Errors bars from the standard deviation are shown

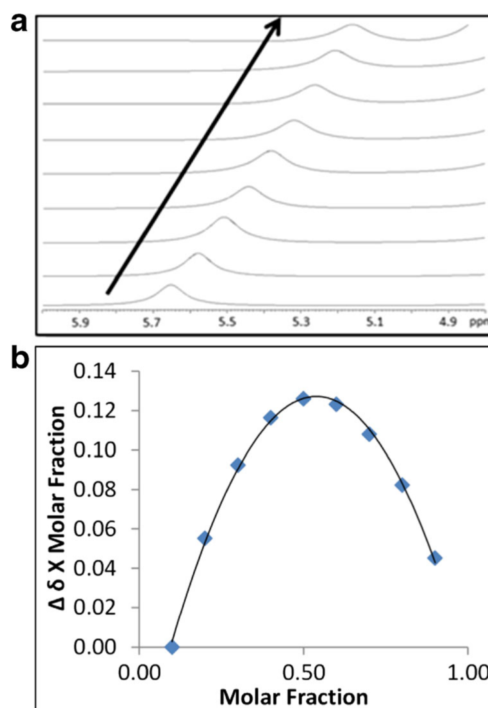


Fig. 4 **a** Stacked ^{1}H NMR spectra of urea upon increasing amounts of hydrogen peroxide (0–2 MEq). **b** Jobs plot to determine the binding stoichiometry between hydrogen peroxide and urea

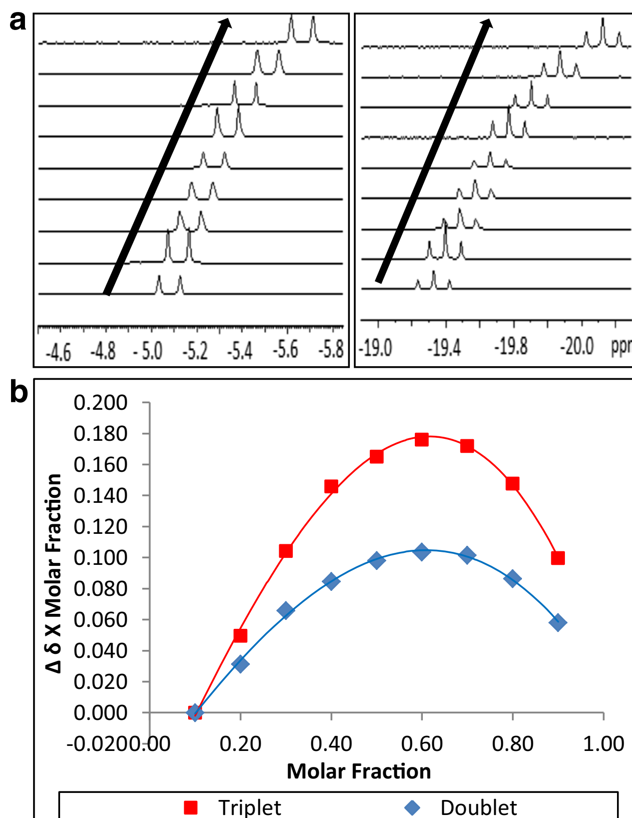


Fig. 5 **a** Stacked ^{31}P NMR spectra of STPP upon increasing the amounts of hydrogen peroxide (0–2 MEq). **b** Jobs plot to determine the binding stoichiometry between hydrogen peroxide and STPP

resulting Job plot revealed the interaction between STPP and hydrogen peroxide to be 1:2 host/guest indicating two molecules of peroxide interact with one molecule of STPP (Fig. 5b). However, when a similar experiment was performed in which STPP was added to urea, no significant change was observed in either the ^{1}H NMR of urea or the ^{31}P NMR of STPP suggesting minimal interaction between these two molecules (Fig. 6). These results suggest that hydrogen peroxide interacts strongly with both urea and STPP, while there is no direct interaction between urea and STPP. One possible model that may explain these results is proposed in Fig. 7 and shows an adduct where two units of carbamide peroxide bind to a central tripolyphosphate anion through the hydrogen peroxide

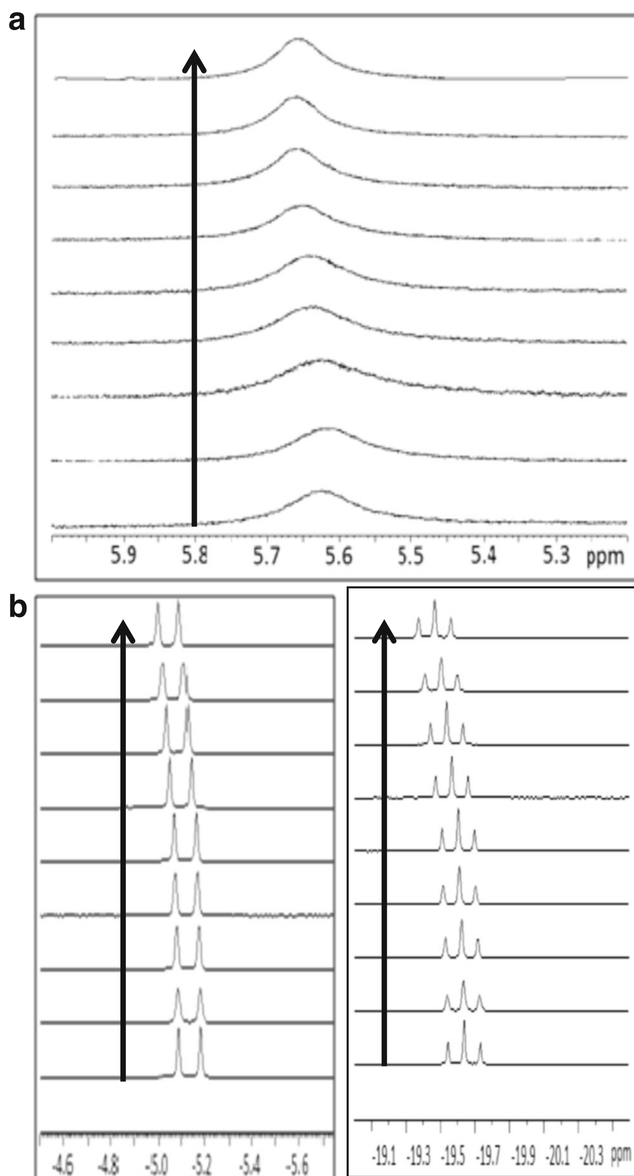


Fig. 6 **a** Stacked ^{1}H NMR spectra of urea upon increasing amounts of STPP (0–2 MEq). **b** Stacked ^{31}P NMR spectra of STPP upon increasing amounts of urea (0–2 MEq)

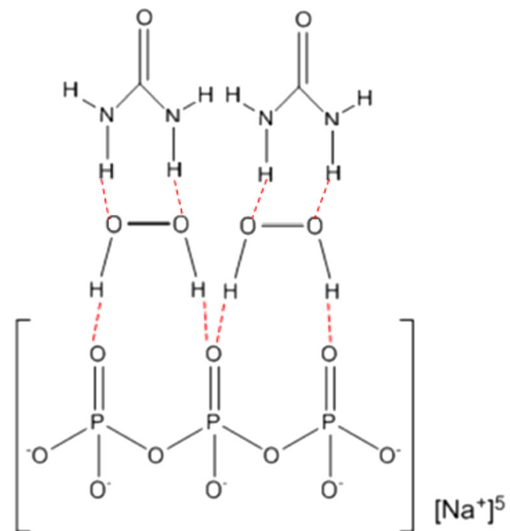


Fig. 7 A possible model for a three-component adduct which allows for direct interaction between hydrogen peroxide: STPP and hydrogen peroxide: Urea but no direct interaction between STPP and urea

unit with no direct interaction between STPP and urea. To test this model, a combination of urea and hydrogen peroxide (i.e. carbamide peroxide) was added directly to STPP (Fig. 8), and

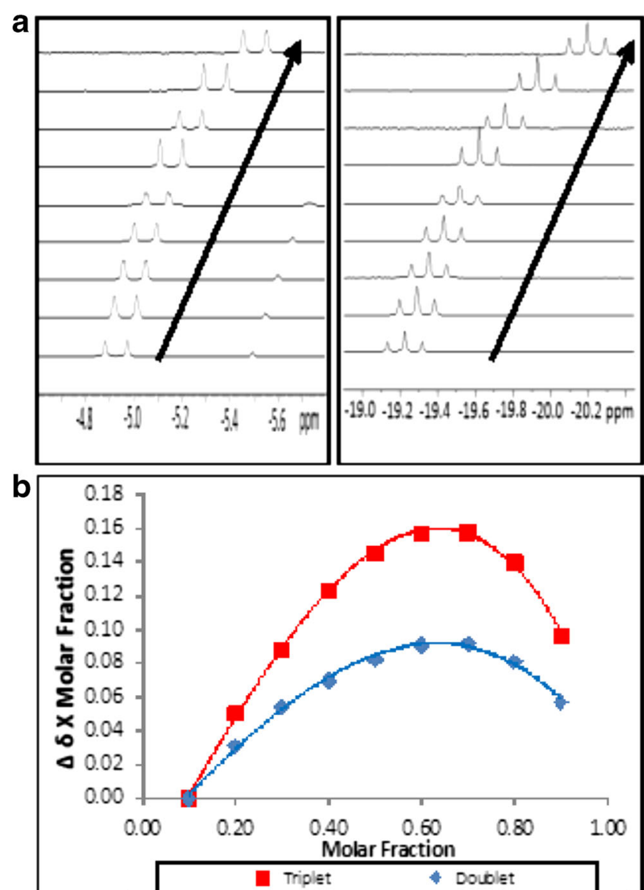


Fig. 8 **a** Stacked ^{31}P NMR spectra of STPP upon increasing amounts of carbamide peroxide (0–2 MEq). **b** Jobs plot to determine the binding stoichiometry between carbamide peroxide and STPP

an almost identical upfield shift was observed in the ^{31}P NMR spectrum as found for the direct addition of hydrogen peroxide to STPP (Fig. 5), suggesting carbamide peroxide interacts with STPP in the same way and to the same extent as hydrogen peroxide alone. Furthermore, when increasing amounts of hydrogen peroxide was added to a solution containing a fixed amount of both urea and STPP, similar changes were observed in both the ^{31}P NMR spectra of STPP (Fig. 9) and the ^{1}H NMR of urea (Fig. 10), as were found for the addition of hydrogen peroxide to STPP and urea alone (Figs. 5 and 6, respectively). These results suggest that hydrogen peroxide does not bind preferentially to either STPP or urea but binds to both, most likely via distinctly different non-competing coordination sites.

Clinical trial A two-way hierarchical ANOVA was performed with repeated measures on the patient over time (baseline and 2 weeks), and the patient nested in the group (group 1, 2, or 3), separately for UL1 and UR3 (Table 1). The outcome variable was either L^*, a^*, or b^* for each ANOVA. The assumptions of the ANOVA were checked by a study of the residuals and

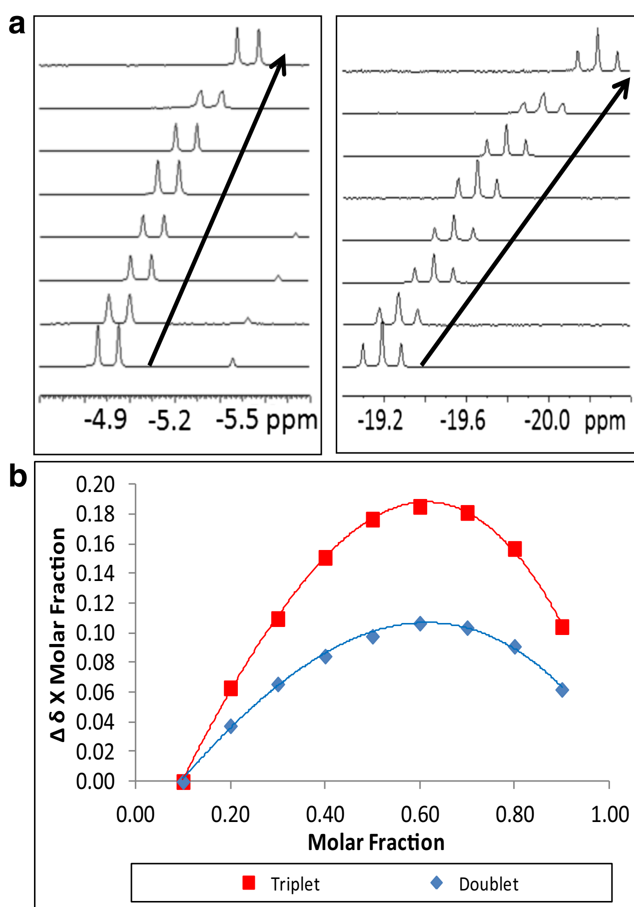


Fig. 9 **a** Stacked ^{31}P NMR spectra of STPP in the presence of urea upon increasing the amounts of hydrogen peroxide (0–2 MEq). **b** Jobs plot to determine the binding stoichiometry between hydrogen peroxide and STPP in the presence of urea

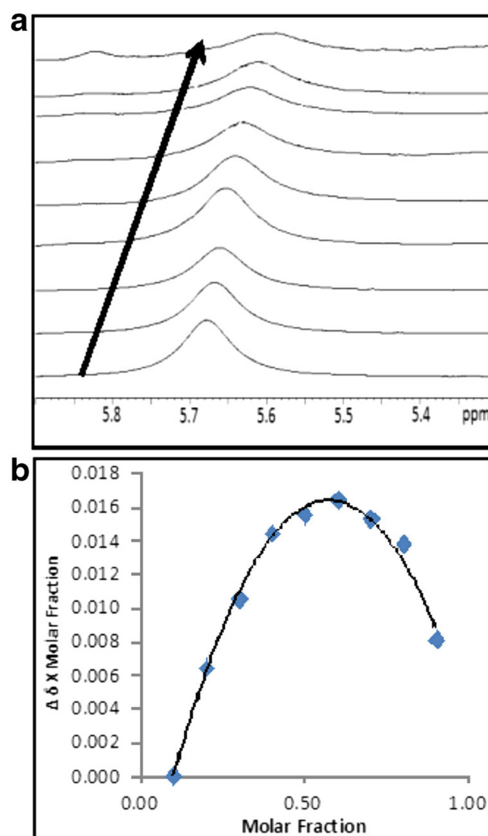


Fig. 10 **a** Stacked ^{1}H NMR spectra of urea in the presence of STPP upon increasing the amounts of hydrogen peroxide (0–2 MEq). **b** Jobs plot to determine the binding stoichiometry of urea and hydrogen peroxide when urea is in the presence of STPP

were found to be satisfactory. There was a significant interaction between time and group for L^* and b^* in the UL1 analysis and for L^* and a^* in the UR3 analysis. Therefore, for consistency, all analyses were followed by a one-way ANOVA comparing the groups at each time and, if there was a significant difference between groups, by Bonferroni post hoc comparisons to determine which groups differed.

The results show that there was no significant difference between the group means at baseline in the one-way ANOVA for any comparison, i.e. for L^*, a^*, and b^* for UL1 and UR3 (Fig. 1a–f). There was also no significant difference between the means of groups 2 and 3 at 2 weeks for any comparison (p>0.999) or between the means of groups 1, 2 and 3 for b^* at 2 weeks for UR3 (p>0.999; Fig. 1f). The 2-week mean of group 1 was significantly less than that of group 2 (p=0.02, p=0.002) and group 3 (p=0.01, p=0.001) for L^* in UL1 and in UR3, respectively (Fig. 1a, d), and the 2-week mean of group 1 was significantly greater than that of group 2 (p=0.02, p=0.02) and group 3 (p=0.008, p=0.04) for a^* in UL1 and UR3, respectively (Fig. 1b, e). The b^* value for the central incisor for group 1 was significantly different to groups 2 and 3 (Fig. 1c). However, there was no significant difference between the two test groups (groups 2 and 3).

Table 1 Mean $L^*a^*b^*$ values and standard deviations for UL1 and UR3

			UL1			UR3		
Time	Group		*L*	*a*	*b*	*L*	*a*	*b*
Baseline	1	*N*	11	11	11	10	10	10
		Mean	71.806	3.374	19.384	70.954	4.985	22.768
		Standard error of mean	1.395	0.597	1.074	0.893	0.415	0.935
	2	*N*	10	10	10	10	10	10
		Mean	74.727	2.395	17.024	70.936	4.601	27.482
		Standard error of mean	0.908	0.24	0.817	0.846	0.308	3.535
	3	*N*	11	11	11	11	11	11
		Mean	73.956	2.511	17.771	71.346	5.011	23.922
		Standard error of mean	1.276	0.367	0.652	0.872	0.035	0.839
		p value (3 groups)	0.24	0.24	0.17	0.94	0.68	0.29
2 weeks	1	*N*	11	11	11	10	10	10
		Mean	71.852	3.319	19.033	70.523	4.789	22.357
		Standard error of mean	1.345	0.592	1.003	0.865	0.408	1.024
	2	*N*	10	10	10	10	10	10
		Mean	76.408	1.686	14.883	74.664	3.351	20.096
		Standard error of mean	0.764	0.181	0.664	0.614	0.272	0.952
	3	*N*	11	11	11	11	11	11
		Mean	76.813	1.775	16.057	74.954	3.646	20.346
		Standard error of mean	1.077	0.189	0.795	0.775	0.213	0.897
		p value (3 groups)	0.005	0.008	0.005	<0.001	0.006	0.21
		Group 1 versus 2	0.02	0.02	0.005	0.002	0.008	
		Group 1 versus 3	0.01	0.02	0.05	0.001	0.04	
		Group 2 versus 3	>0.999	<0.999	>0.999	>0.999	>0.999	

Discussion

When whitening gels such as Carbamide Plus are applied to the teeth, the hydrogel matrix becomes swollen with saliva which effectively dilutes the contents contained within. Given the importance of pH on the kinetics of hydrogen peroxide dissociation, we began this study by investigating the effect of dilution on solution pH. This revealed a significant increase in ΔpH for Carbamide Plus compared to carbamide peroxide. Indeed, at 5 % *w*/*v*, the pH of the Carbamide Plus solution was some 0.70 pH units greater than carbamide peroxide solution at the same concentration. This significant increase in solution pH upon dilution of Carbamide Plus can be directly attributed to the presence of STPP which is otherwise absent in carbamide peroxide. It is postulated that this increase in solution pH upon dilution increases the rate of dissociation of hydrogen peroxide Carbamide Plus facilitating the bleaching process.

NMR spectroscopy is routinely used to investigate binding interactions in host–guest systems [28–30]. In particular, strong intermolecular hydrogen bonding interactions between a 'host' and 'guest' can significantly influence the degree of shielding surrounding a nucleus which manifests itself as a change in chemical shift. Results from the NMR analysis revealed direct interactions between urea and hydrogen peroxide as well as between urea and STPP, with minimal interaction between STPP and hydrogen peroxide. Furthermore, the stoichiometry of these associations was 1:1 for urea and hydrogen peroxide and 2:1 for urea and STPP, suggesting two molecules of hydrogen peroxide bind to STPP while at the same time also binding to one molecule of urea each, as shown in Fig. 7.

The clinical study also produced some interesting results. The 2-week mean of group 1 was significantly less than that of groups 2 and 3 for L^* in UL1 and in UR3, respectively (Fig. 1a, d), and the 2-week mean of group 1 was significantly greater than that of groups 2 and 3 for a^* in UL1 and UR3, respectively (Fig. 1b, e). This means that there were significant differences between control and test groups for L^* and a^*. The b^* value for the central incisor for group 1 was significantly different to groups 2 and 3 (Fig. 1c). This difference between the control and test groups indicates a reduction in yellowness of the test groups. However, there was no significant difference between the two test groups (groups 2 and 3) indicating that there was no difference in tooth-

whitening between 5 % (Carbamide Plus) and 10 % carbamide peroxide. Conversely, there was no significant difference between the means of groups 1, 2, and 3 for b^* at 2 weeks for UR3 (Fig. 1f). Canines are known to be particularly yellow teeth and are bulky in shape. These factors appear to have challenged the tooth-whitening ability of both the 5 % Carbamide Plus and 10 % carbamide peroxide to reduce the yellowness. However, it is not uncommon for dentists to recommend continued treatment for canine teeth after the initial 2 weeks in order to allow all teeth to reach the same target shade.

As the hydrogen peroxide concentration of whitening gels has been linked with problems such as tooth sensitivity and gingival irritation, the possibility of using lower hydrogen peroxide concentration yet retaining whitening efficiency has obvious benefits. The side effects of external tooth bleaching have been well-described in a multi-centre practice-based prospective study by Bruzell et al. [9]. They compared home versus in-office whitening and found the two most frequently occurring side effects were sensitivity and gingival irritation. One of the treatment-related predictors of side effects was bleaching concentration: higher sensitivity is experienced with higher concentrations of bleaching agent.

Basting et al. [31] also reported a significant prevalence of tooth sensitivity during tooth-whitening using at home 20 % carbamide peroxide agent when compared to 10 % carbamide peroxide or in-office treatment, and this was attributed to high concentration or time/length the agent was in contact with dental structures.

The efficiency of Carbamide Plus at reduced hydrogen peroxide concentration has been attributed to the presence of STPP which is otherwise absent in carbamide peroxide. The presence of STPP, in combination with hydrogen peroxide and urea, results in a significant increase in solution pH upon dilution. It is hypothesised that this pH rise facilitates a more rapid dissociation of hydrogen peroxide resulting in an improved whitening efficiency when compared to carbamide peroxide. An NMR study into the behaviour of these three components in solution revealed a direct interaction between hydrogen peroxide with both urea and STPP with little interaction between urea and STPP. Based on these results, a proposed structure for Carbamide Plus was suggested where two moles of carbamide peroxide bind to a single STPP unit through the hydrogen peroxide component with no direct interaction between urea and STPP. This new formulation offers the possibility of using significantly lower amounts of hydrogen peroxide to achieve similar whitening effect. This may bring additional benefits to the user in terms of reduced tooth sensitivity gingival irritation and also to deliver this in an alkaline environment thus minimising any adverse effects that may occur with low pH products [32].

Conclusions

A new tooth-whitening product Carbamide Plus containing urea, hydrogen peroxide, and STPP as active components containing 5 % hydrogen peroxide has been shown to be as effective as the commercially available carbamide peroxide containing 10 % hydrogen peroxide. The presence of STPP, in combination with hydrogen peroxide and urea, results in a significant increase in solution pH upon dilution. It is hypothesised that this pH rise facilitates a more rapid dissociation of hydrogen peroxide resulting in an improved whitening efficiency when compared to carbamide peroxide. There were no statistically significant differences between Carbamide Plus and 10 % carbamide peroxide in tooth-whitening at 2 weeks following daily wear of tooth-whitening trays for 2 h/day.

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