Scientific Documentation

ivoclar vivadent:
passion vision innovation

Table of contents

1. Introduction

1.1 Subjective perception of tooth colour

A smile is one of the most important non-verbal but communicative social skills there is, and many studies show that the colour of the teeth plays a major role in the perception of dental attractiveness [1, 2]. Accordingly, a large percentage of the adult population is dissatisfied with the colour of their teeth [1, 3] and seeks improvement.

Satisfaction of personal tooth colour was investigated in a study involving 180 subjects aged between 13 and 64 years [4]. Despite the age group: 55 to 64, having significantly darker/yellower teeth than the age group: 13 to 17, both groups expressed similar levels of dissatisfaction with their own tooth colour. About a third of each group was satisfied with their tooth colour. It was speculated that different expectations exist within the age groups that may affect tooth-colour satisfaction. Individuals seem to seek whiter teeth within their own peer group but not necessarily the whitest teeth possible.

The subjective first-person response for having teeth bleached was investigated in a study involving 50 adults testing self-administered peroxide-containing tooth whitening products [5]. Tooth colour was measured objectively before and after the treatment, and a questionnaire was completed after the treatment. It was found that the subjective response to the bleaching result was significantly correlated with changes in b*, but not in L* or a*. Thus, the yellow-blue shift seems to be of primary perceptual importance to the user of tooth bleaching products.

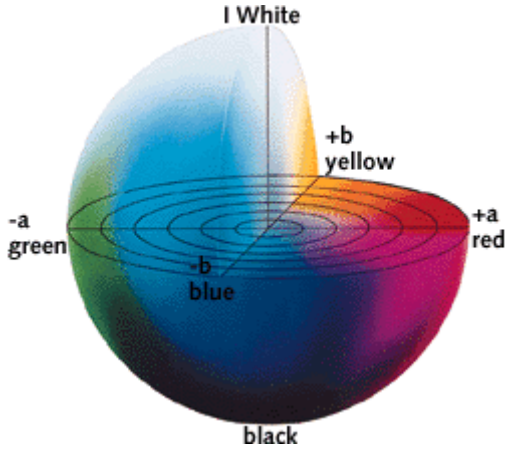


Fig. 1: The L - a* - b* space provides a three-dimensional colour space, where the a*-b* axes form one plane to which the L* axis is orthogonal. In the colour space, the achromatic dimension of colour signals i.e. lightness value (L*) is represented as well as the chromatic via the yellow-blue axis (b*) and the red-green axis (a*). Picture taken from [6].*

1.2 Natural tooth colour and discolouration

The primary perception of the natural tooth colour is a combination of its optical properties. When light encounters a tooth, some of it will be transmitted through the tooth, some of it will be reflected from the surface and some will be absorbed and scattered within the dental tissue. Illuminating light follows a highly irregular light path through the tooth before it emerges at the surface of incidence and reaches the eye of the observer [1].

With increasing age, the tooth colour becomes darker and more yellow due to a number of different factors: As the pulp ages, it shrinks leaving secondary dentin in its wake. The surrounding dentin becomes harder and darker. The thickness of the enamel decreases due to natural wear, and the dentin colour begins to dominate the tooth colour. The colour will increase in a* and b* values, whereas the L* value will decrease. This shift in tooth colour is natural and cannot be reversed, i.e. it cannot be influenced by bleaching.

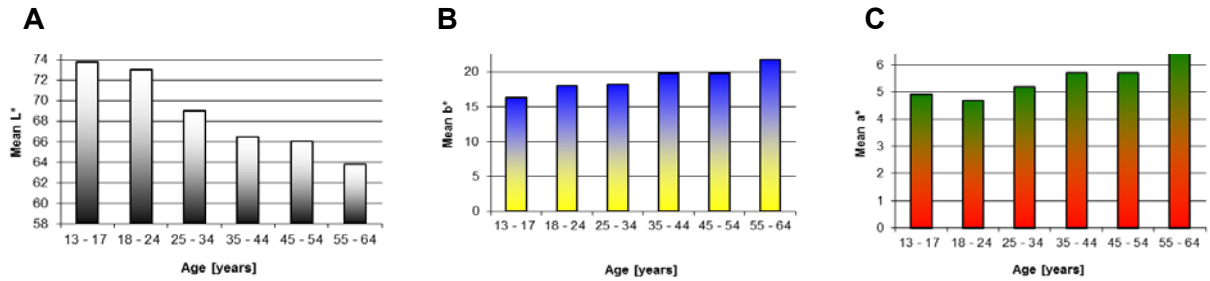


Fig. 2: Age-dependent shift of L (Diagram A), a* (Diagram C) and b* values (Diagram B) in a sample population of 180 people. Modified from [4].*

Tooth discolouration is traditionally classified according to the location and aetiology of the stain. Extrinsic stains are caused by external deposits, whereas intrinsic stains are embedded in the dental hard tissue (for a review see [7]).

Extrinsic stains are incorporated into the pellicle or may penetrate through cracks into the enamel. These stains are typically caused by chromogens contained in food, beverages and tobacco products. They are very treatable with bleaching agents.

Intrinsic stains can either be of an endogenous nature like pulpal haemorrhagic products, or can be incorporated from exogenous sources such as medication (e.g. tetracycline derivatives, fluoride or phenolic compounds found in root canal sealing materials). It has been shown that these kinds of stains can be lightened by extended bleaching procedures.

However, discolouration caused by developmental defects like amylogenesis or dentinogenesis imperfecta cannot be treated by bleaching.

1.3 Measuring tooth colour

To assess the efficacy of a bleaching treatment, the tooth colour must be accurately determined before and after the treatment. Currently several different measurement techniques are employed (Fig. 3), for example, shade tab assignment, photography or spectroscopy. All of these techniques give an output that needs to be transformed numerically. Only this numerical transformation provides the investigator with a tool that can be used to express clinical success, i.e. the achieved colour shift.

In commercial shade guides, the individual tabs are ordered according to the manufacturer's recommendation and a ranking number is assigned. One of the most commonly used shade guides is the Vitapan classical shade guide. As with most other shade guides, which are arranged according to the manufacturer's recommendations, the intervals between the adjacent pairs of tabs are irregular and there are some reversals in the general trend from dark to bright (ΔL*) (see Table 1). The difference in the overall colour change to the neighbouring tab can vary from 0.99 to 6.4. This high variation hampers the validity of the assigned rank numbers as a tool to express the clinical efficacy of a bleaching procedure.

	B1	A1	B2	D2	A2	C1	C2	D4	A3	B3	D3	A3.5	B4	C3	A4	C4
No	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
L*	78.9	79.6	76.7	75.3	76	74.2	71	71.9	75.4	72.6	74.1	72.3	71.8	68.8	68.6	64.8
a*	-1.76	-1.61	-1.62	-0.54	-0.08	-1.26	-0.22	-1.03	1.36	0.47	0.62	1.48	0.5	-0.01	1.58	1.59
b*	12.33	13.05	16.62	13.47	16.73	12.56	16.72	17.77	19.61	22.34	16.14	21.81	22.15	16.68	21	18.66
ΔL*		-0.7	2.9	1.4	-0.7	1.8	3.2	-0.9	-3.5	2.8	-1.5	1.8	0.5	3	0.2	3.8
ΔE		0.99	4.61	3.61	3.38	4.7	5.39	1.61	5.42	3.64	6.4	5.74	1.15	6.16	4.52	4.45

Table 1: Classical arrangement of the Vitapan shade tabs used in bleaching studies. The L a* b* values are taken from [8] and ΔE was calculated as follows:* $\Delta E = (\Delta L^2 + \Delta a^2 + \Delta b^2)^{1/2}$

Nevertheless, shade guides are a valid tool for assessing tooth colour. They have been used successfully for decades and are an easy tool that can be handled reliably. Using a shade guide also means that the colour is assessed by the human eye, which ultimately is also the arbiter of clinical success. The usefulness of shade guides can also be improved by changing the numeric transformation i.e. by assigning the L*a*b* values to the tabs. This leads to a more precise evaluation of the clinical efficacy of bleaching treatments.

Tooth colour can be determined more precisely using a chromameter/spectrometer. The colour of a small part of the tooth is evaluated using a device that reads the refracted wavelength directly. This reduces the considerable subjective component involved when colour is assessed by an investigator, plus shade attribution is not limited to the tabs but is extended to a continuous colour space. On the other hand, colour measurement with a device is complex: To produce a meaningful result, an alignment device must be used. If this device does not fit properly, it can lead to measuring errors. Also the expressed L* a* b* coordinates can differ from brand to brand of measuring device. When comparing the data on the Vitapan classical shade guide, the published L* a* b* values of Li [9] and O'Brien [10] differ quite substantially.

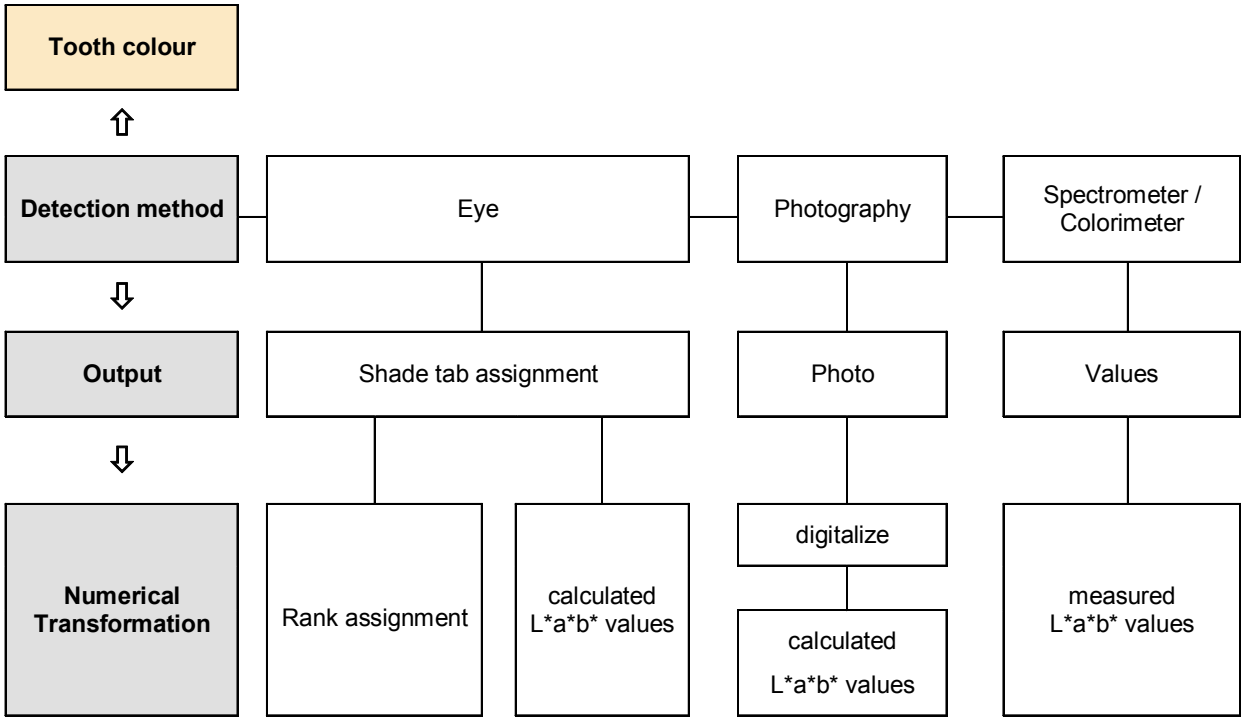


Fig. 3: Methods for determining tooth colour and their numerical transformation

1.4 How do tooth bleaching agents work?

Dental whitening agents are supplied in a variety of forms. Gel products seem to be the most widely used. They can be applied to the teeth directly or by means of dental trays. Furthermore, strips are offered, which are worn directly on the teeth. Some whitening products come in pen form and the bleaching agent is "drawn" on the tooth. Only Ivoclar Vivadent supplies a tooth whitening varnish that is painted on with a brush. The varnish sets to form a layer on the tooth surfaces, where the whitener can take effect.

The VivaStyle range comprises the following products:

VivaStyle Paint On Plus, a varnish-based bleaching agent containing hydrogen peroxide as the active ingredient. The concentration of peroxide is 6% dissolved in ethanol. After the application of the product on the tooth surface, the ethanol evaporates and leaves behind a layer of varnish that is enriched with peroxide. With this technique it is possible to deliver a

higher concentration of peroxide to the tooth surface than that contained in the original formulation.

VivaStyle Gel, which is available in three different concentration levels: 10%, 16% and 30%. These products contain carbamide peroxide as the active ingredient. Carbamide peroxide is a 1:1 complex of urea and hydrogen peroxide, in which 1 g carbamide peroxide is equivalent to 0.36 g hydrogen peroxide. Therefore, the carbamide content of VivaStyle 10% is equivalent to 3.6% hydrogen peroxide. The content of VivaStyle 16% is equivalent to 5.8% hydrogen peroxide and that of VivaStyle 30% is equivalent to 10.8% hydrogen peroxide.

Ultimately, the active compound of the VivaStyle bleaching products is hydrogen peroxide.

Once applied on the tooth surface, the peroxide decays. This decay is triggered by the elevated temperature (body temperature), pH changes and the presence of catalysts, such as metal ions originating from deposits on the tooth, or enzymes from the saliva (peroxidases and catalases). Depending on the catalyst, hydrogen peroxide decays to oxygen and various highly reactive radicals (hydroxyl or perhydroxyl radicals) that can either oxidize unsaturated double bonds or reduce chromogenic metal oxides. Organic stains are typically characterized by conjugated double bonds giving those molecules a colour. These unsaturated double bonds are prone to being oxidized and are converted in a cascade of reactions to colourless hydroxylated compounds. In contrast however, the radicals are not able to interact with the mineral content of the dental hard tissue.

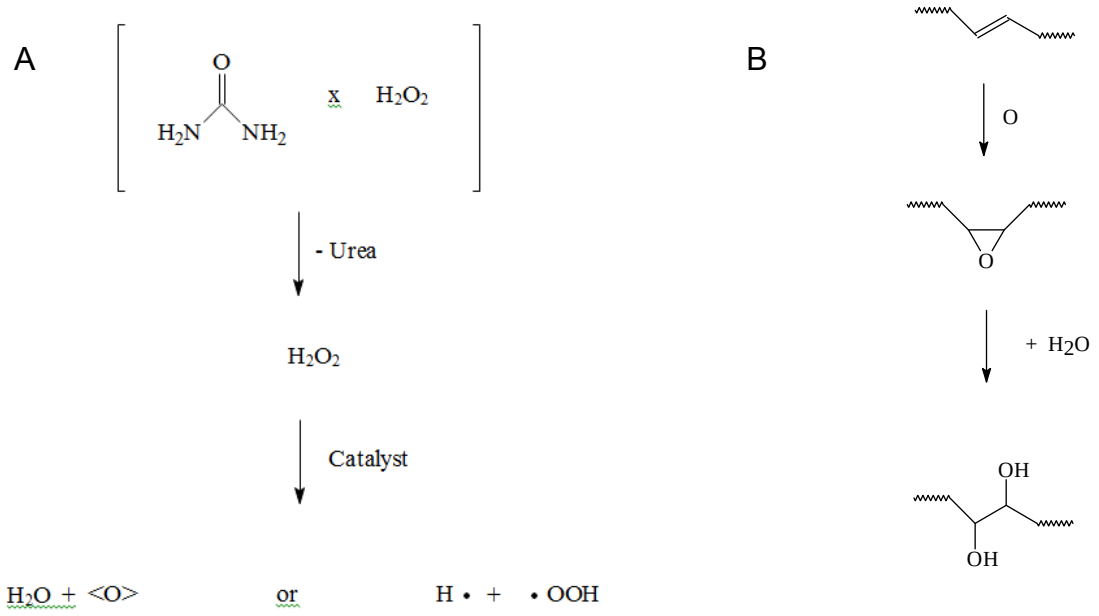


Fig. 4: Mode of action: Carbamide peroxide decays to urea and hydrogen peroxide. Depending on the catalyst, hydrogen peroxide decays to various radicals (panel A). These radicals (singlet oxygen for example) attack the chromogenic materials and oxidize them to colourless compounds (panel B).

1.5 What can be achieved with bleaching agents?

Bright white teeth like those of international celebrities cannot be achieved with any of the bleaching products available today. Teeth can only be whitened to the lightest natural shade that the teeth possessed before they were stained. By nature, teeth are slightly yellowish. This is a state that cannot be changed by bleaching.

Some manufacturers of bleaching products recommend that the bleaching agent be subjected to a strong light after its application. This is claimed to activate the whitening product and therefore improve the result. However, studies have shown that this “light activation” does not provide any real benefits. On the contrary, it can give rise to unpleasant side effects, such as tooth sensitivity and gum irritation. Moreover, the elevated temperature produced by the lamp could harm the pulp [11, 12]. In addition, it has been found that dental bleaching trays do not have to be equipped with reservoirs [13].

The duration of the whitening results can be influenced by the individual. The lighter tooth shade can be maintained by refraining from or reducing the consumption of foods and beverages that could stain the teeth, for example, red wine, tea, curry and blueberries. Smoking may also stain the teeth more quickly.

2. Technical data

VivaStyle® 10%, VivaStyle® 16%

Tooth whitening gel

Standard - Composition (in weight %)

	VivaStyle 10%	VivaStyle 16%
Glycerin	50 – 75	25 - 50
Aqua	10 - 25	10 - 25
Urea (Carbamide) Peroxide	10	16
Carbomer	1 - 5	5 – 10
Potassium Nitrate	1 - 5	1 – 5
Sodium Hydroxide	1 - 5	1 – 5
Aroma	0.1 - 1.0	0.1 – 1.0
EDTA	0.1 - 1.0	0.1 – 1.0
Sodium Saccharin	---	0.1 – 1.0

Physical properties

EN ISO 28399:2011 Dentistry – Products for external tooth bleaching (ISO 28399:2011)

			VivaStyle 10%	VivaStyle 16%
		Specification	Example value	Example value
Active ingredient: Carbamide peroxide	%	7.0 – 11.0 11.2 – 17.6	10.0 ---	--- 16.2
Reduction of micro hardness of the surface	%	≤ 10	1.4	0.1
Surface erosion		< 3 x Positive control	No erosion measurable	No erosion measurable

Other properties

pH Value		≥ 4.0	6.9	6.9

VivaStyle® 30%

Tooth whithening gel

Standard - Composition (in weight %)

Glycerin, Aqua	53 - 67
Urea Peroxide	30
Potassium Nitrate, Carbomer, Sodium Hydroxide	3 - 15
Disodium EDTA, Aroma	0.2 – 2

Physical properties

EN ISO 28399:2011 Dentistry – Products for external tooth bleaching (ISO 28399:2011)

		Specification	Example value
Active ingredient: Carbamide peroxide	%	21 - 33	29.7
Reduction of micro hardness of the surface	%	≤ 10	No reduction measurable
Surface erosion		< 3 x Positive control	No erosion measurable
Other properties			
pH Value		≥ 4.0	7.3

VivaStyle Paint On Plus

Tooth whitening varnish

Standard-Composition	**(in weight %)**
Varnish (Alcohol, Ethylcellulose, Aqua)	> 93.0
Hydrogen Peroxide	6.0
Panthenol, Aroma	< 1.0

Physical properties

EN ISO 28399:2011 Dentistry – Products for external tooth bleaching (ISO 28399:2011)

		Specification	Example value
Active ingredient: Hydrogen peroxide	%	5.9 – 6.5	6.3
Reduction of micro hardness of the surface	%	≤ 10	2.5
Surface erosion		< 3 x Positive control	No erosion measurable

3. Studies

3.1 VivaStyle Paint On Plus

3.1.1 Dr A. Peschke, Ivoclar Vivadent Schaan (Liechtenstein)

The aim of this pilot study was to examine the safety and efficacy of VivaStyle Paint On Plus in a small number of subjects (n = 7). The product was applied 14 times for 10 minutes according to the manufacturer's instructions, and the bleaching effect was assessed with the help of the Vita shade guide.

Even though the cut-off criterion for inclusion in the study was a relatively light tooth colour (A2), an average lightening of almost three shade tabs was achieved (2.9 tabs).

A clinically insignificant irritation of the gingival tissue was observed in most of the subjects. Hypersensitivity did not occur.

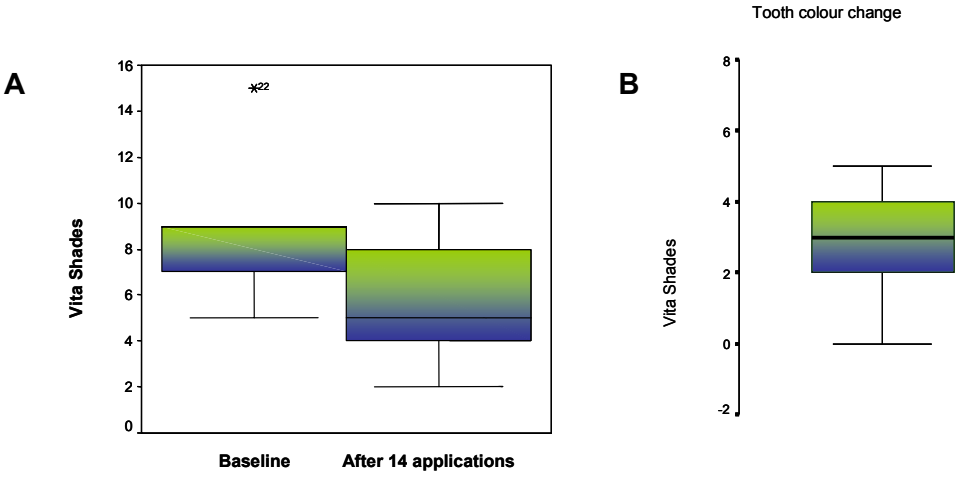


Fig. 5: Change in the tooth colour of the central incisor: A: Distribution of the numerically transformed Vita shade tabs before and after bleaching (14 x 10 min). B: Distribution of the bleaching results expressed in Vita shades.

3.1.2 Prof Dr T. Attin, University of Göttingen (Germany)

Two aspects were investigated in this study:

- Clinical efficacy and safety of VivaStyle Paint On Plus
- Effectiveness of VivaSens desensitizer as a means of preventing bleaching-related hypersensitivity

Sixty-seven subjects were randomly allocated to two groups. One group was pretreated with VivaSens, while the other group, which did not receive any pretreatment, served as the control. The members of both groups applied VivaStyle Paint On Plus twice a day for 10 minutes over a period of one week. After this time, the change in the tooth colour as well as any side effects were examined.

No differences in the bleaching results of the groups who had or had not used VivaSens were determined (2.7 ± 1 vs. 2.82 ± 0.85 shade tabs). The criterion for inclusion in the study was the tooth colour A2 or darker. This colour is quite light for bleaching studies; usually at least A3 (or darker) is required for bleaching studies. The analysis of the group with tooth colour A3 and darker showed an average lightening of 3.2 shade tabs (2.8 shade tabs for all the subjects).

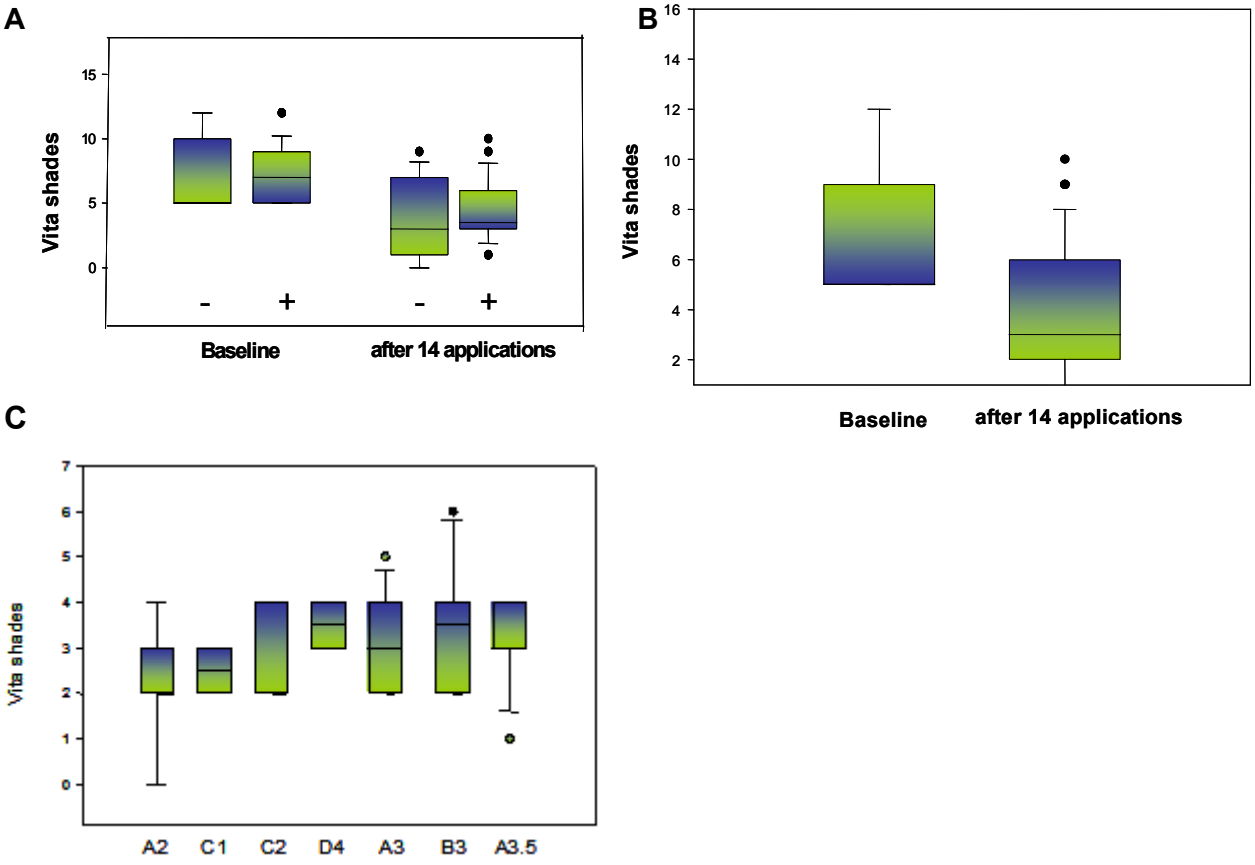


Fig. 6: Bleaching efficacy of VivaStyle Paint On Plus. A: Distribution of the tooth colours before and after the bleaching procedure, classified according to the treatment groups (-) = without VivaSens, (+) = with VivaSens. B: Distribution of the tooth colours before and after the bleaching treatment of all the subjects. C: Lightening in shade tabs according to the initial colour.

The occurrence of sensitivity was determined in a test using blown air. A quarter of the subjects exhibited tooth sensitivity even before the treatment. In the group which did not receive pretreatment with VivaSens, the number of people showing tooth sensitivity increased by 15%, while only one person (= 3%) reported tooth sensitivity in the group treated with VivaSens. About 80% of the subjects reported irritation of the gingiva. None of the irritations were of clinical significance.

	Group without VivaSens (n = 33)		Group with VivaSens (n = 34)	
Hypersensitivity prior to bleaching	24.2 %	n = 8	26.5 %	n = 9
Hypersensitivity after the end of the bleaching procedure	39.4 % **Δ = 15.2 %**	n = 13 Δ = 5	29.4 % **Δ = 2.9 %**	n = 10 Δ = 1

3.1.3 Prof Dr I. Krejci, University of Geneva (Switzerland)

Study objective: The aim of this study was to establish the tooth whitening efficacy of VivaStyle Paint On Plus and to determine how long the bleaching results last.

Method: Ten people participated in the study. VivaStyle Paint On Plus was used at three appointments within two weeks: It was applied five consecutive times each for 10 minutes. At baseline and after the first week and after six months, digital photos were taken of the upper central incisors. The Vita shade guide was used as a reference. Furthermore, the CIE L*a*b* values of the incisors were spectrophotometrically determined using the SpectroShade device. The results were used to establish the colour changes ΔE during and after the whitening treatment.

Results: The changes in the colour parameters showed that the lightening process was a success. A comparison of the shade before and after the bleaching treatment revealed a statistically significant difference in L*, a* and b*. The whitening results lasted for at least six months: Figure 6 shows that ΔE3, which represents the colour change in the period between the end of the bleaching treatment and the subsequent six months, is very small and significantly different from ΔE2 and also ΔE1, which are both based on the initial shade.

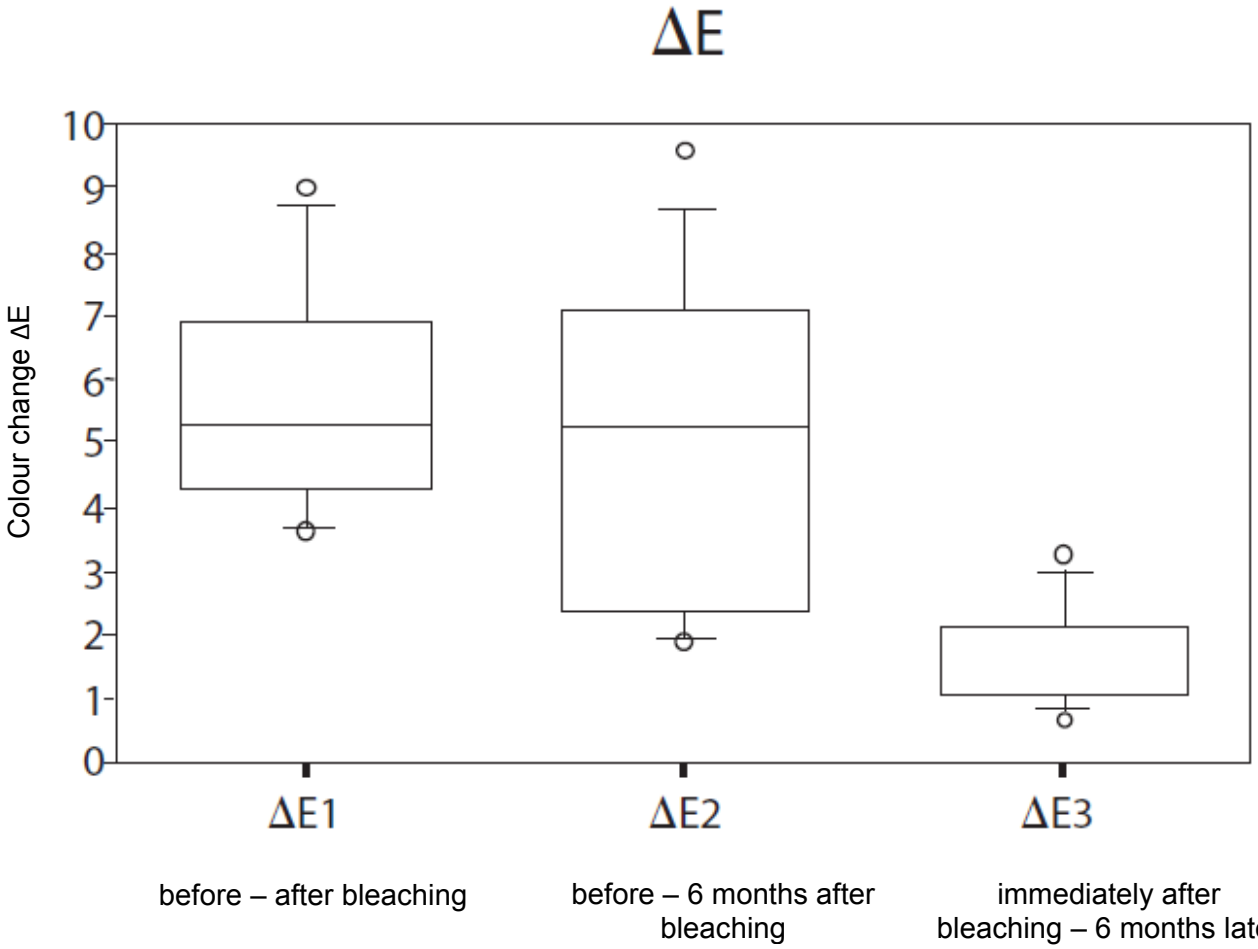


Fig. 7: Beaching effect of VivaStyle Paint On Plus at various times. ΔE1: Difference in colour before and immediately after the bleaching treatment. ΔE2: Difference in colour before and six months after the bleaching treatment. ΔE3: Difference in colour immediately after the bleaching treatment and after six months.

Conclusion: VivaStyle Paint On Plus lightens the teeth for a period of at least six months.

Reference: [14]

3.1.4 Ass. Prof. Dr A. Duarte Sola Pereira da Mata, Institute of Health Sciences Egas Moniz, Monte Caparica (Portugal)

Study objective: This trial examined the efficacy of VivaStyle Paint On Plus in lightening teeth.

Method: Six people participated in the study. VivaStyle Paint On Plus was used in the dental practice at two different appointments within a two-week period. At each appointment, the product was applied six consecutive times for 10 minutes. Digital photos were taken of the upper central incisors at the beginning and after the treatment. The tooth colour was determined with a Vita shade guide. In addition, the satisfaction of the test subjects was surveyed with a questionnaire. At the same time, the occurrence of hypersensitivity was evaluated.

Results: The tooth whitening results of all the test subjects were considered to be successful. Colour changes from 7 to 13 shade tabs on the Vita scale (see graph) were achieved. None of the participants reported any tooth sensitivity. Overall a high level of acceptance of the whitening varnish was recorded on the part of the test users.

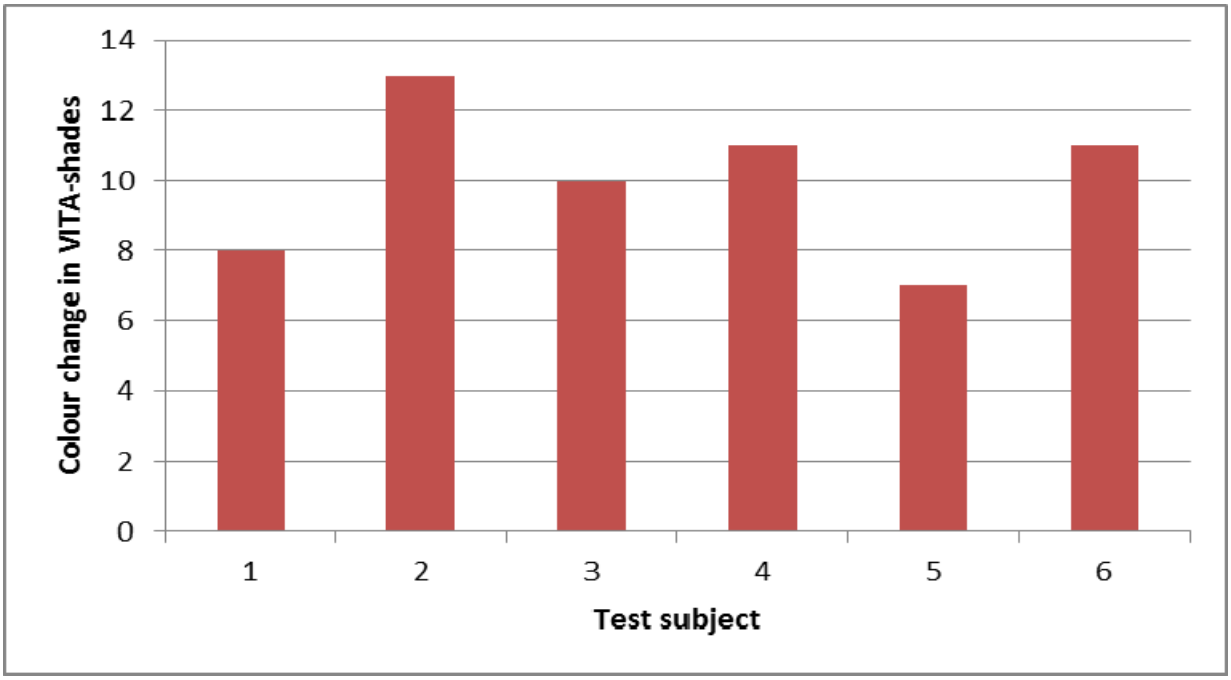


Fig. 8: Individual colour changes after bleaching with VivaStyle Paint On Plus. The graph shows the shade change on the Vita scale before and after bleaching in test subjects 1-6.

Conclusion: VivaStyle Paint On Plus effectively whitens teeth.

Reference: [15]

3.2 VivaStyle gel products

Effective mid-2013, the VivaStyle gel products will feature a new, improved formulation. The gels have been subjected to a number of *in vitro* examinations, which are required by the standard for bleaching products (ISO 28399).

A large amount of clinical data on the effectiveness and safety of the predecessor products is available. Since the active ingredient (carbamide peroxide) and its concentration have remained unchanged, this information is therefore applicable to the gel products featuring the improved formulation.

3.2.1 In vitro investigations

3.2.1.1 Influence of bleaching on dental enamel - Microhardness

Study objective: This study examined the influence of tooth whitening with VivaStyle 10%, 16% and 30% on the hardness of the dental enamel in accordance with the requirements of ISO 28399.

Method: Bovine teeth were embedded in resin and then cut and polished to produce cylindrical test specimens with a diameter of 4 mm. The samples were immersed in water and then cleaned with ethanol and dried. Their baseline hardness was then established. Ten specimens each were treated for 60 minutes with the three different VivaStyle gels (10%, 16%, 30%). Subsequently, the products were removed with a soft brush. The samples were rinsed with water and then placed in artificial saliva at 37°C. This treatment was repeated daily over a period of two weeks. After the last bleaching treatment, the samples were placed in saliva for another 24 hours before the microhardness was tested.

Results: VivaStyle gels lead to only minimal changes in the microhardness of the enamel (max 2.5% decrease). According to the standard, up to 10% is acceptable.

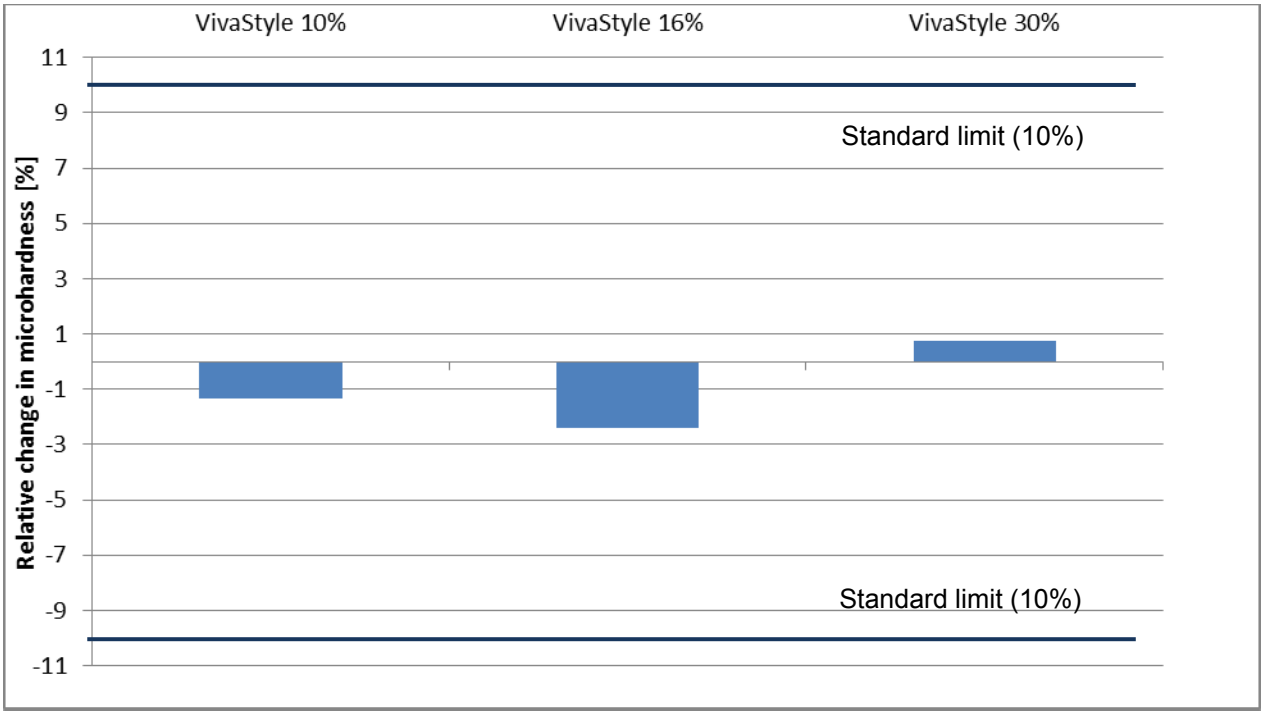


Fig. 9: Change in the microhardness of dental enamel after treatment with VivaStyle gels. Tested according to ISO 28399. Ivoclar Vivadent R&D, 2012.

Conclusion: VivaStyle gel products have little influence on the hardness of dental enamel.

Reference: Ivoclar Vivadent AG, Schaan, 2012

3.2.1.2 Influence of bleaching on dental enamel - Erosion

Study objective: The aim of this study was to investigate whether or not tooth whitening with VivaStyle 10%, 16% and 30% causes enamel erosion according to ISO 28399.

Method: Bovine teeth were embedded in a resin and ground down to the enamel or dentin. The edges of the tooth surfaces were covered with adhesive tape, leaving only an exposed strip of 2-3 mm. Six teeth were used in each group. Deionized water served as the negative control and citric acid as the positive control.

The test specimens (enamel and dentin) were treated with the bleaching agents and the control solutions for 60 minutes daily for two weeks. Subsequently, the gels and the solutions were rinsed off and the specimens were temporarily stored in artificial saliva at 37 °C.

After the different treatments, the adhesive tape was taken off the enamel and any adhesive residue was removed with acetone. The teeth were placed in water until their surface profile was measured.

Results: The specimens treated with the positive control showed significant erosion of the enamel and dentin. In contrast, the VivaStyle gel products – like the negative control – did not cause any erosion of the tooth structure.

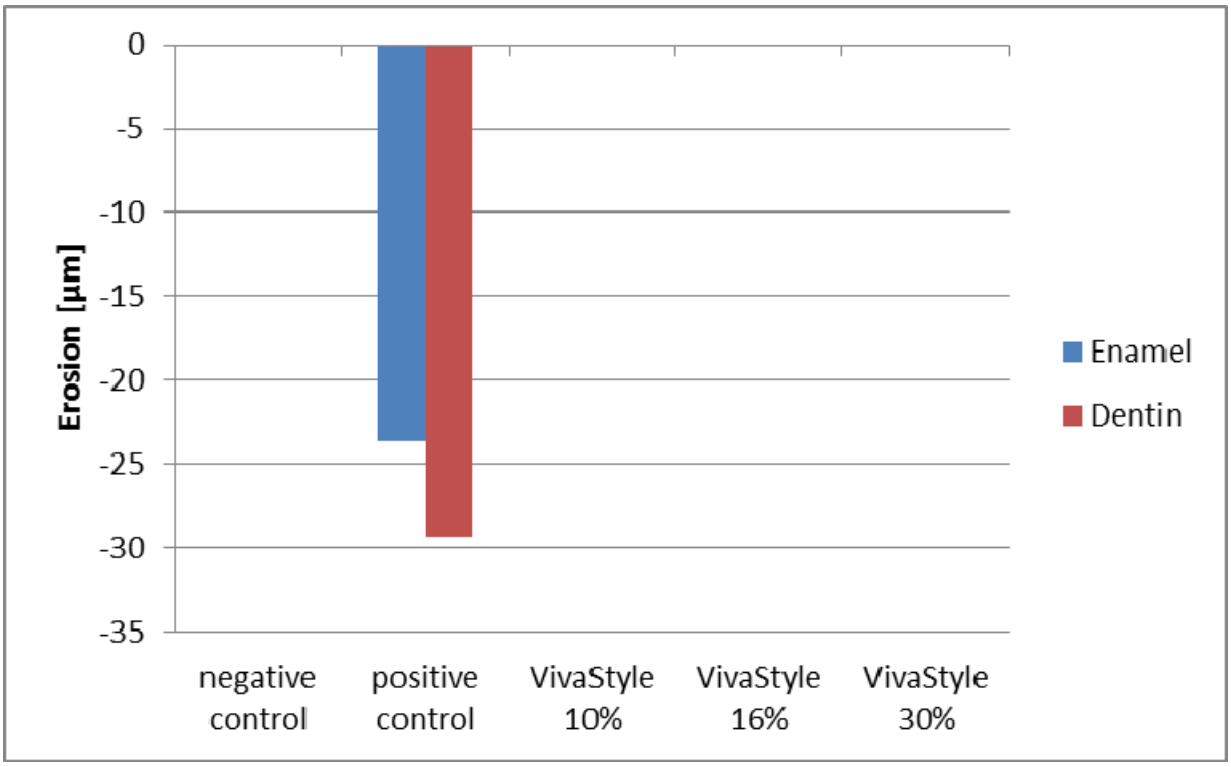


Fig. 10: Erosion of dental enamel and dentin after treatment with VivaStyle gel products. Tested according to ISO 28399. Ivoclar Vivadent R&D, 2012.

Conclusion: VivaStyle gels do not cause erosion.

Reference: Ivoclar Vivadent AG, Schaan, 2012

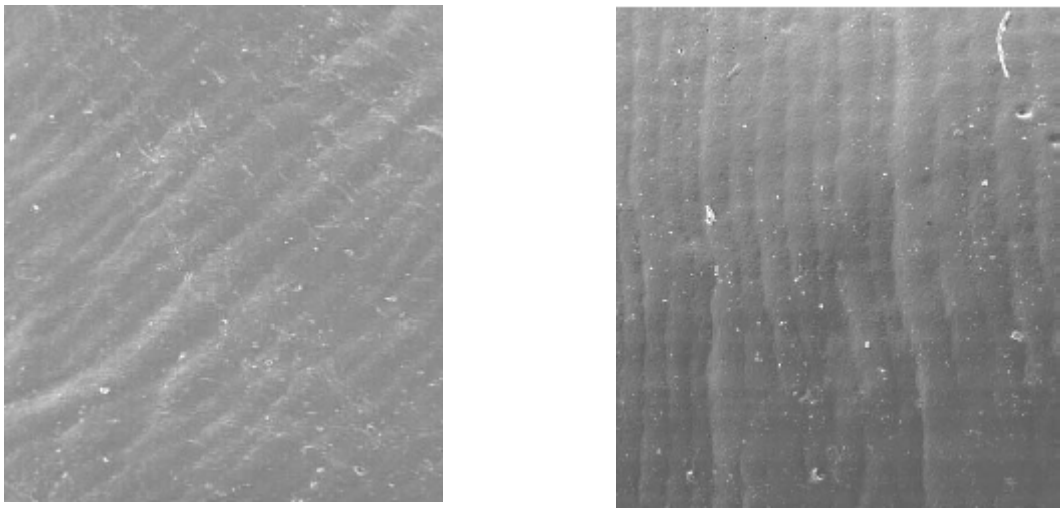
3.2.2 Clinical experience - VivaStyle 10%

3.2.2.1 A. Berga Caballero, University of Valencia (Spain)

Study objective: This trial examined the influence of tooth whitening with VivaStyle 10% on dental enamel.

Method: In two groups of ten test subjects each, VivaStyle 10% or the bleaching product FKD (Laboratorios Kin; 3.5% hydrogen peroxide) was used. The treatment lasted 2-3 hours daily for 28-33 days. Before the treatment and after its completion, replicas of the tooth surfaces were fabricated, which were examined with scanning electron microscopy.

Results: The scanning electron microscope images showed undamaged enamel with a normal surface structure, both before and after the whitening treatment with VivaStyle 10%.



Before bleaching

After the application of VivaStyle 10%

Fig. 11: Scanning electron microscope image of the dental enamel after the treatment with VivaStyle 10%. Taken from [16].

Conclusion: VivaStyle 10% does not damage the dental enamel.

Reference: [16]

3.2.2.2 C. Hannig, D. Linder, T. Attin, University of Freiburg (Germany)

Study objective: In this trial, tooth whitening with VivaStyle 10% carbamide peroxide was compared to that of Whitestrips (Procter & Gamble, 6% hydrogen peroxide).

Method: A total of 47 people participated in the examination. The study was randomized and designed as a single-blind investigation in two parallel groups. The VivaStyle group wore the loaded trays for one hour, once a day. The comparison group used Whitestrips twice a day for 30 minutes each. The tooth colour (L*a*b values) was determined before and after the treatment. Furthermore, the participants were re-examined up to eight weeks after the whitening treatment in order to determine the biocompatibility.

Results: The tooth colour improved significantly after two weeks in both groups. The brightness of the teeth increased, while the yellowish appearance decreased. In 13% of the cases, transient irritation of the gums was recorded, while in 22%, hypersensitivity of the teeth was observed. After eight weeks however, these side effects had disappeared. VivaStyle induced more gingival irritation, but less tooth sensitivity than Whitestrips. No difference between the two bleaching methods was noted, even though two subjects using Whitestrips stopped the treatment after five days due to subjective discomfort. Treatment with VivaStyle was rated “comfortable” by the subjects, whereas Whitestrips were rated “slightly uncomfortable”. Moreover, significantly more subjects in the group using Whitestrips complained about the taste of the product (five vs. one in the VivaStyle group). This may be the reason why 91% of the subjects using VivaStyle recommend the treatment in contrast to only 61% of the Whitestrips group. This is a statistically significant difference. Furthermore, more users of VivaStyle than users of Whitestrips would repeat the treatment.

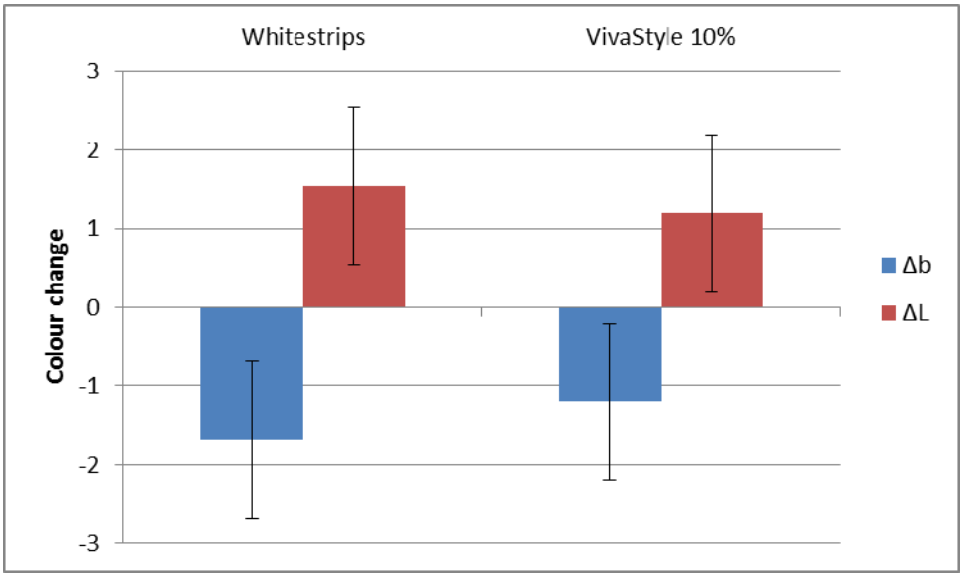


Fig. 12: Colour change after treatment with Whitestrips and VivaStyle 10%. Modified according to [17].

Conclusion: VivaStyle 10% achieved significant whitening after a two-week application.

Reference: [17]

3.2.2.3 C-P. Ernst, T. Wiechers, B. Willershausen, University of Mainz (Germany)

Study objective: The aim of this trial was to investigate tooth whitening with VivaStyle 10% and 16% compared with a placebo.

Method: A total of 30 people took part in the study. Each test group comprised ten participants (VivaStyle 10%, VivaStyle 16%, placebo gel). The study was carried out in double-blind form. The subjects wore the loaded trays over night for ten days. The tooth colour was measured with the Chromascop shade guide before and after the treatment.

Results: In both the VivaStyle groups, the tooth colour appeared up to three shade tabs lighter after the treatment. The incisors were shown to whiten more easily than the canines. The placebo gel did not have any lightening effect.

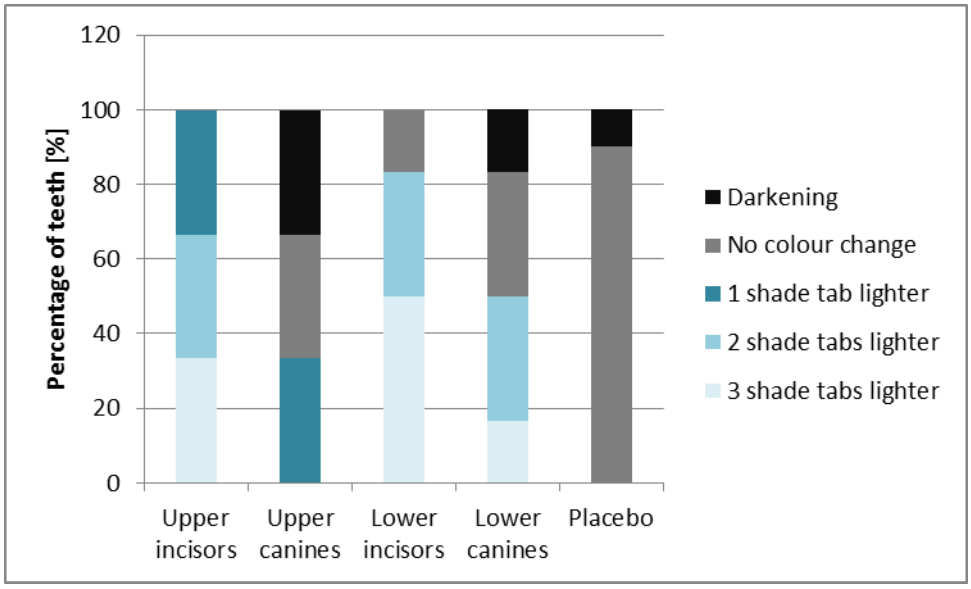


Fig. 13a: Colour change of individual teeth after treatment with VivaStyle 10%. Modified according to [18, 19].

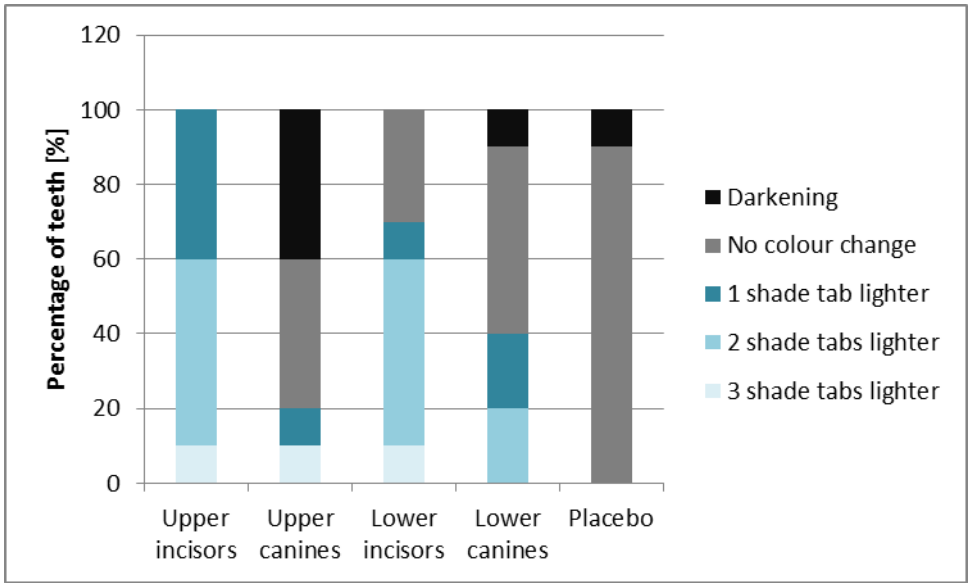


Fig. 13b: Colour change of individual teeth after treatment with VivaStyle 16%. Modified according to [18, 19].

Conclusion: VivaStyle 10% and 16% effectively whiten anterior teeth.

Reference: [18, 19]

3.2.2.4 D. Lindner, C. Hannig, T. Attin, University of Göttingen (Germany)

Objective of study: This study examined the durability of the tooth whitening results achieved with VivaStyle 10% compared to that of Whitestrips (6% hydrogen peroxide).

Method: A total of 42 people took part in the study. The trial was designed as a randomized single-blind investigation. The participants were evenly divided into two groups of 21 people according to the L values. The VivaStyle group wore the loaded trays for one hour once a day. The comparison group used Whitestrips twice a day for 30 minutes each. The tooth colour (L*a*b values) was determined before and after the treatment on the basis of digital photographs of the facial surfaces of the upper incisors and canines. The tooth colour was checked after two weeks, two months and six months.

Results: Both products were found to lighten the tooth colour. After six months, the teeth were still lighter and the yellow component of the tooth colour was lower than before the treatment. No difference between the two bleaching methods was noted.

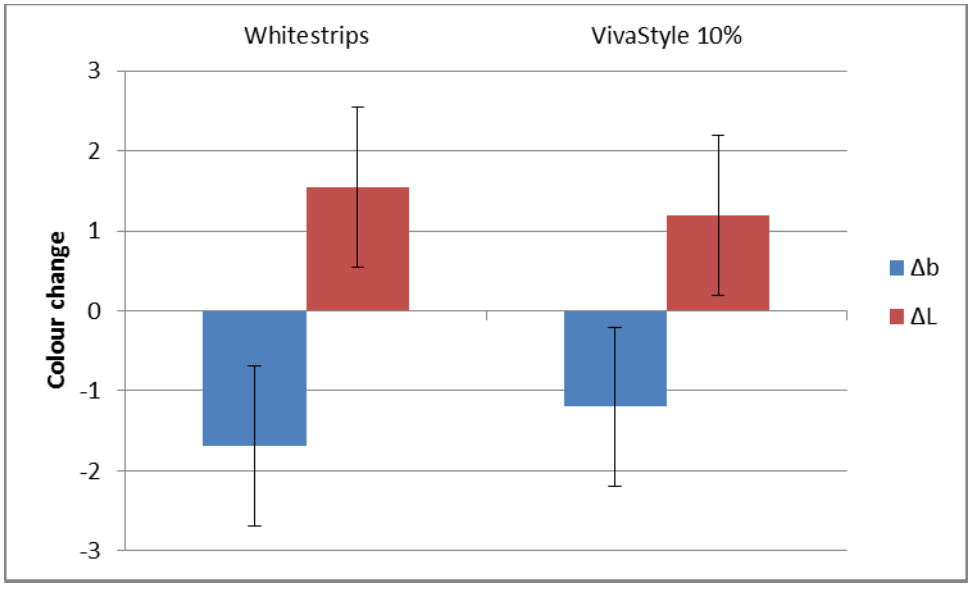


Fig. 14: Colour change after treatment with VivaStyle 10%. Results after six months compared with the initial situation. Modified according to [20]

Conclusion: VivaStyle 10% produces long-lasting tooth whitening results

Reference: [20]

3.2.2.5 S. Heintze, Ivoclar Vivadent AG, Schaan (Liechtenstein)

Study objective: The aim of this trial was to examine the tooth whitening results of VivaStyle 10%.

Method: A total of 10 people took part in the study. VivaStyle 10% was applied in each jaw with a tray which was worn over night for seven nights. The upper teeth were treated first, followed by the lower teeth. The tooth shade was determined with the Chromascop. Follow-up examinations took place after seven and 14 days and one month after the treatment.

Results: The teeth in the upper and in the lower jaw showed an average lightening result of three shade tabs. Tooth hypersensitivity (in 8 out of 10 subjects) and irritation (in 3 out of 10 subjects) did occur, but subsided very quickly. One month after the treatment, the teeth of six out of the 10 subjects had become one shade darker.

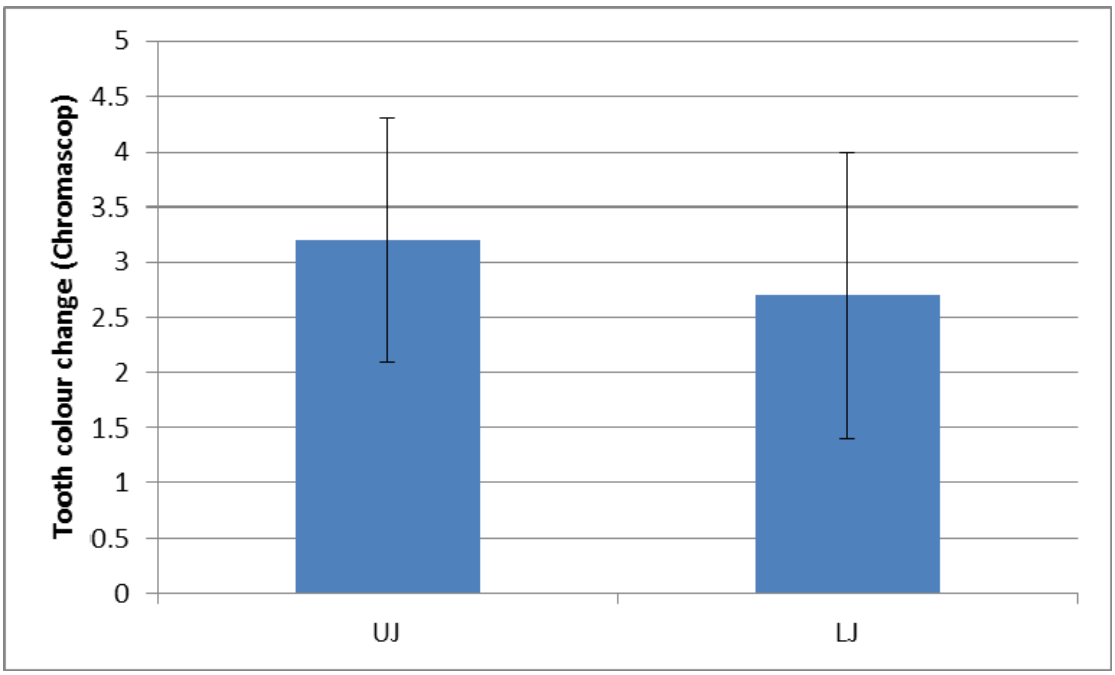


Fig. 15: Colour change after treatment with VivaStyle 10% in the upper jaw (UJ) and in the lower jaw (LJ). Results compared with the initial situation. Modified according to [21]

Conclusion: One week after the treatment with VivaStyle 10%, the teeth were considerably lighter both in the upper and the lower jaw.

Reference: [21]

3.2.2.6 K. Malkiewicz, E. Jodkowska, Medical University of Warsaw (Poland)

Study objective: This trial examined the changes in tooth colour in the course of tooth whitening with VivaStyle 10%.

Method: A total of 20 people took part in the study. VivaStyle 10% was used for two hours daily for a period of 14 days. The shade analyzer system from Ivoclar Vivadent was used to determine the tooth colour. The tooth shade was determined before the bleaching treatment. A second reading was taken after seven days and a third one after 14 days.

Results: The treatment with VivaStyle 10% brightened the teeth. After only seven days, the teeth were visibly lighter. The tooth colour continued to become lighter during the second week of the treatment. At the same time, the yellow component of the tooth colour decreased.

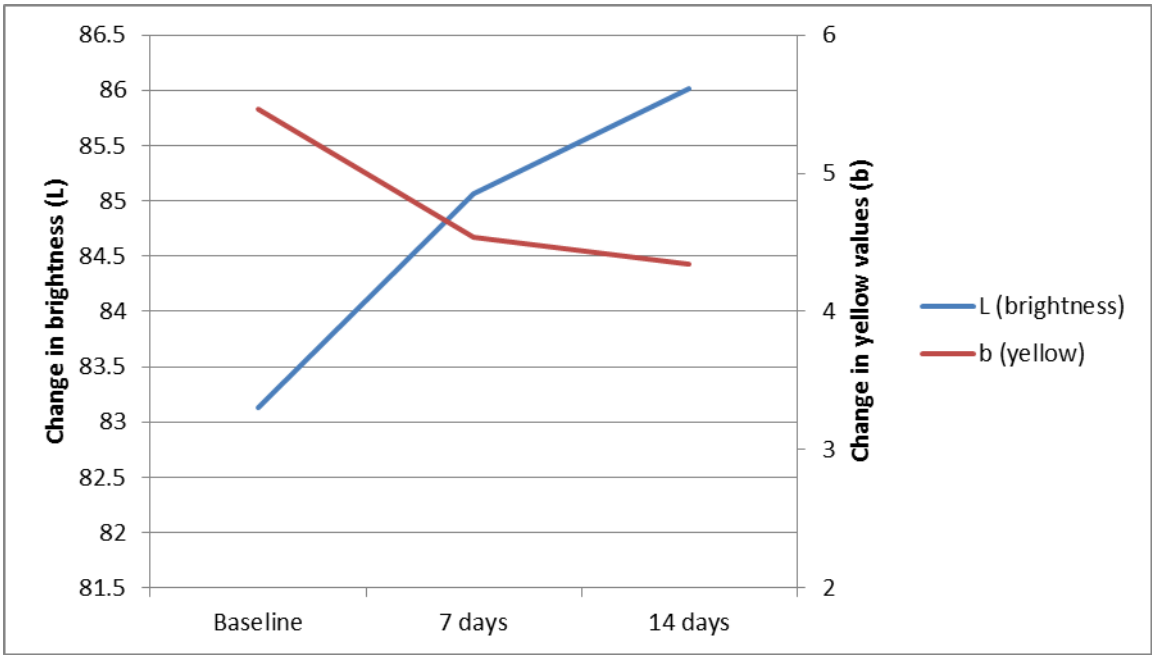


Fig. 16: Change in brightness and yellow values of teeth during 14-day treatment with VivaStyle 10%. Modified according to [22]

Conclusion: After the two-week treatment with VivaStyle, the teeth were lighter and less yellow in appearance.

Reference: [22]

3.2.3 Clinical experience – VivaStyle 16% and 30%

3.2.3.1 Prof. J. M. Hernandez, University of Seville (Spain)

Study objective: This study examined the change in tooth colour during a course of whitening with VivaStyle 16% and 30%.

Method: Thirty people used VivaStyle 16% for 14 days. Another 35 people received two 30-minute treatments with VivaStyle 30%. The tooth colour was established with the Chromascop (L*a*b* values) on one incisor and one canine from each dental arch. Furthermore, the condition of the gums, the sensitivity of the teeth and the satisfaction of the patients was surveyed (by means of questionnaires). Follow-up examinations took place after seven and 14 days.

Results: The treatment with VivaStyle 16% produced a statistically significant and visible improvement in the tooth colour, including an increase in brightness and a reduction in the red and yellow components. The 14-day application regime achieved better results than the seven-day course.

VivaStyle 30% was shown to be significantly more effective if it was used twice rather than just once. The treatment with this product also improved the tooth brightness and the colour in terms of the red and yellow components.

Both groups did not reveal any difference between the tooth types (incisors vs. canines).

Light hypersensitivity occurred in conjunction with the use of VivaStyle 16% in 60% of the participants. Transient gum irritation was experienced by 36% of the subjects. After the first treatment with VivaStyle 30%, irritation was reported by 71% of the participants, while almost 90% were affected after the second course. Twenty-six percent of the test subjects complained about tooth sensitivity after the first treatment and 40% after the second treatment.

Nevertheless, the participants rated the treatment and its results as very good: 96% found VivaStyle 16% to be comfortable to use; VivaStyle 30% was deemed to be comfortable by 77%. All the people (100%) who used VivaStyle 16% were satisfied with the results. In the case of VivaStyle 30%, almost 90% of the users were satisfied.

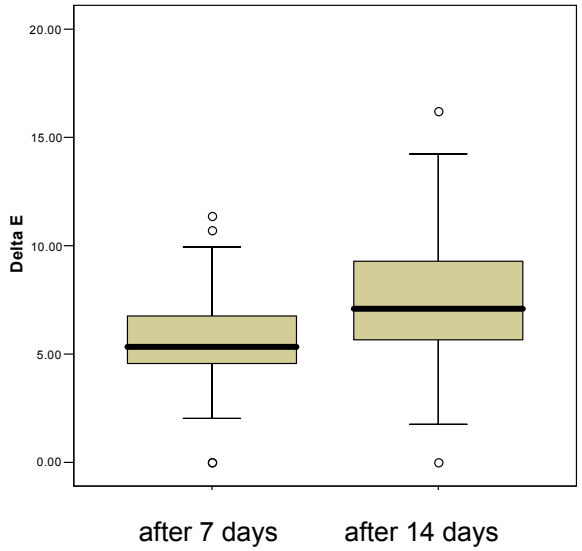


Fig. 17a: Colour change after 7- and 14-day treatment with VivaStyle 16%. Modified according to [23]

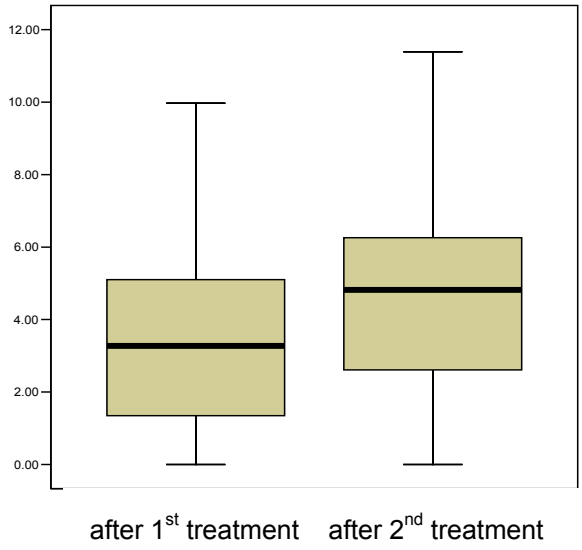


Fig. 17b: Colour change after 1st and 2nd treatment with VivaStyle 30%. Modified according to [23]

Conclusion: VivaStyle 16% and 30% visibly lighten the teeth. The test subjects found the products to be comfortable to use and they were satisfied with the results.

Reference: [23]

3.2.3.2 Prof. A. Mata, Institute of Health Sciences Egas Moniz, Monte Caparica (Portugal)

Study objective: The aim of this trial was to examine the clinical efficacy of VivaStyle 30%.

Method: The study involved a randomized, double-blind trial among 60 participants. The tooth colour was evaluated by means of a Vita shade guide under standardized light conditions. After professional tooth cleaning, the teeth of the test subjects were either treated with

VivaStyle 30% or a placebo. This treatment was repeated once. The shade stability was checked after one, three and six months.

Results: The treatment with VivaStyle 30% lightened the teeth by more than three shade tabs. After six months, a relapse of about half a shade tab was recorded in one case.

Transient hypersensitivity and gum irritation were experienced by several of the participants. Three subjects stopped the treatment because of excessive hypersensitivity.

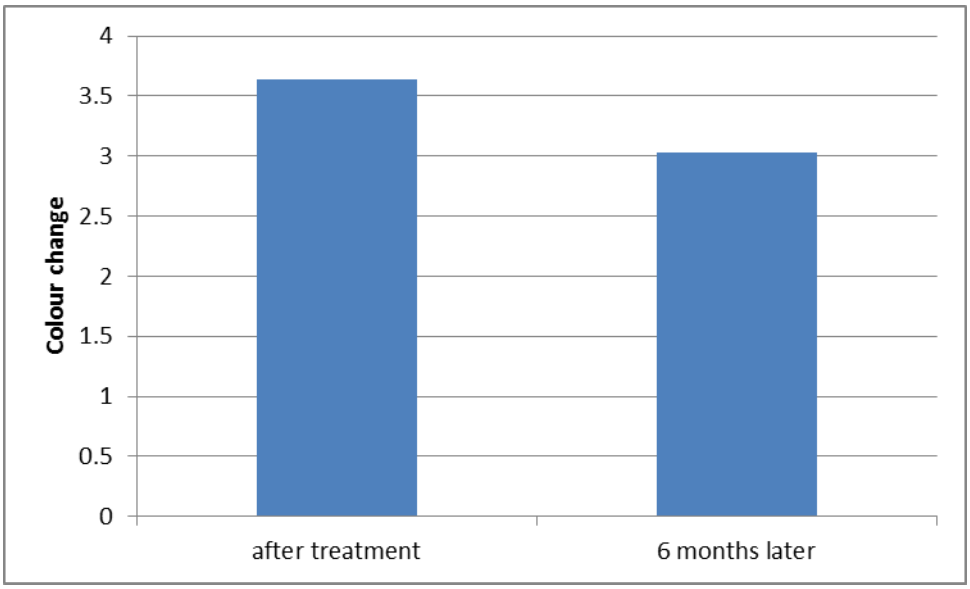


Fig. 18: Colour change immediately following the treatment with VivaStyle 30% and 6 months later. Modified according to [24]

Conclusion: VivaStyle 30% produces significant lightening results which last for at least six months.

Reference: [24]

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4. Biocompatibility

4.1 Introduction

VivaStyle Paint On Plus contains ethanol, ethyl cellulose, D-Panthenol and mint flavour, as well as 6% hydrogen peroxide.

VivaStyle 10%, 16% and 30% contain glycerine, water, carbamide peroxide, carbomers, potassium nitrate, sodium hydroxide, flavour and disodium EDTA. VivaStyle 16% additionally contains saccharin.

The inactive ingredients are widely used as carriers for the active substances in approved drugs and are considered to be safe. Ethyl cellulose is not metabolized, as humans do not have cellulose enzymes; if orally ingested, it is automatically excreted. D-Panthenol is a pro-vitamin used in cosmetic products, toothpaste and mouth rinses at concentrations of up to 1.5%. If resorbed, it is metabolized to Vitamin B5. The dried varnish components of VivaStyle Paint On were extracted with artificial saliva and the extract was evaluated for its cytotoxicity (XTT) and genotoxicity (AMES test). The extract did not exhibit any cytotoxicity or genotoxicity [1-2].

In comparison to the other ingredients of the VivaStyle products, hydrogen peroxide and carbamide peroxide show acute toxicity. For this reason, the toxicological assessment has been focused on peroxides.

4.2 Toxicity

Hydrogen peroxide is a substance that is naturally found in the human body. The average concentration in human blood is 0.3 mM and in the eye 2.4×10^{-5} M [3]. Carbamide peroxide decays to urea and hydrogen peroxide (H_2O_2). The toxicity of hydrogen peroxide is associated with its ability to form radicals and release oxygen.

4.2.1 Acute toxicity

The LD_{50} for oral application of carbamide peroxide in rodents (rat and mouse) is ~3300 mg/kg [4] and of hydrogen peroxide 600 – 1600 mg/kg [5]. The maximum amount of peroxide applied per treatment is about 70 mg, which corresponds to a dose of about 1-2 mg/kg.

Nevertheless, acute toxicity has been reported in humans that have accidentally ingested hydrogen peroxide [5-7]. In most of these reports, small children were affected that had accidentally ingested peroxide-containing household products (35% hydrogen peroxide). Since VivaStyle Paint On Plus and VivaStyle 10% and 16% are take-home products, clear measures must be taken to keep them out of the reach of children.

In an animal study [8], high amounts of carbamide peroxide (>150 mg 10% carbamide peroxide per kg body weight) were administered to rats by a stomach gavage. The rats were killed after 1 or 24 h and the organs were examined. The results showed ulceration of the gastric mucosa in the one-hour animals, while the lesions seemed to be healing in the 24-h animals. No systemic toxicity could be detected (analysis of kidneys and liver). Hence, transient irritation of the gastric mucosa is to be expected if large amounts of VivaStyle are accidentally ingested. This is indirectly confirmed by reports from Procter & Gamble, where patients have accidentally swallowed teeth whitening strips, leading to very minor and transient gastrointestinal symptoms (referenced in [5]).

4.2.2 Cytotoxicity

The *in vitro* cytotoxicity of carbamide peroxide-containing tooth whitener (VivaStyle 16%) was evaluated in a study using an MTT assay [9]. Its cytotoxicity is comparable to other tooth whiteners and is correlated to the H_2O_2 content. Similar studies have been published in the

literature [5,7,10]. These findings are not unexpected, since H_2O_2 is a highly reactive compound, thus enabling it to act as a bleaching agent.

Considering the mode of clinical application, the level of exposure and the high turnover of H_2O_2 in the oral cavity [3,11], the observed cytotoxicity does not constitute a significant risk *in vivo* [12-13].

4.2.3 Genotoxicity

The genotoxicity of tooth whiteners has been investigated in a number of studies, which have been reported in the literature. Some of these investigations were initiated by Ivoclar Vivadent [14-15]. The overall data available so far show that H_2O_2 is only genotoxic in *in vitro* systems (for extensive reviews see [1,5,7]). When metabolic activation is incorporated into *in vitro* systems or when tested in animals, H_2O_2 is non-genotoxic. This also applies to long-term *in vivo* studies with Chinese hamsters [16].

A number of national safety authorities have evaluated the carcinogenicity of hydrogen peroxide or bleaching products (US Food and Drug Administration [17], European Union, Institute of Health and Consumer Protection [18], European Union, Scientific Committee on Cosmetic Products and Non-food products intended for Consumers [5], Health Council of the Netherlands [19]). They have come to the conclusion that there is no significant evidence of carcinogenicity in humans originating from H_2O_2.

4.2.4 Sensitization

Hydrogen peroxide is a substance produced by the human body and thus does not exhibit an allergic potential. This is supported by epidemiological data [18]. Current data on H_2O_2 do not provide adequate evidence that hydrogen peroxide is a skin sensitizer [5].

4.3 Tissue compatibility

4.3.1 Oral soft tissue

It is highly likely that VivaStyle will come into contact with oral soft tissue. Oral mucous membrane irritation tests in animals (rats, hamsters and rabbits) using tooth whiteners containing 22% CP for up to six weeks did not show any clinically relevant evidence of irritation [5]. This corresponds to the clinical experience with tooth whiteners of a normal concentration, with which clinically irrelevant irritation of the gingiva regularly occurs.

4.3.2 Oral hard tissue

The microhardness and surface morphology of human enamel have been evaluated *in vitro* following ADA guidelines after using a 10% carbamide peroxide concentration (VivaStyle). Under the conditions of the study, it was concluded that the treatment for a total of 360 h did not adversely affect the microhardness and the surface morphology of human enamel ([20]. For reviews see [5-7]. See also chapter 3.2.1.

4.3.3 Other tissue

Skin irritation tests on rabbits using tooth whiteners containing H_2O_2 concentrations of up to 8% (corresponds to a carbamide peroxide concentration of about 24%) produced negative results [5]. Both peroxides caused irritation when they came in contact with the eyes [5].

4.4 Literature on biocompatibility

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