



# Over-the-Counter Tooth Whitening Agents: A Review of Literature

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There is an increased accessibility of over-the-counter (OTC) whitening agents with very little data in the literature regarding their effectiveness. This review was done to determine their effectiveness of the predominant OTC whitening agents from 2006 until 2018 where a comparison of each agent was made with a placebo, no treatment or with other OTC whitening agents. The major categories of OTC whitening agents such as dentifrices, whitening strips and paint on gels. Dentist prescribed bleaching applied at home and in-office bleaching studies and studies that demonstrated whitening products to participants were excluded. Articles were searched for in the databases of Medline (Ovid), PubMed, the Cochrane Library and Cochrane Central Register of Controlled Trials. Twenty-four articles were included in the systematic review and the quality of studies was determined by the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) ranking criteria. Compared to other OTC, strips are reported to be effective. Two studies determined whitening strips to be effective. Whitening strips have been shown to be effective when compared with placebos and other OTC whitening agents. Dentifrices are effective in changing the shade of the tooth "by removing extrinsic stains" when compared to a placebo and non-whitening dentifrices, but they are not as effective in comparison to whitening strips. There is a lack of evidence with regards to the effectiveness of paint-on gels. While there is some evidence that OTC can alter shade in the short term, there is a need for better-designed studies.

Key Words: teeth bleaching, teeth whitening, over-the-counter.

## Introduction

In the developed world patients are placing a stronger interest on the aesthetic appearance of their teeth. This paradigm shift coupled with increased accessibility to over-the-counter (OTC) has resulted in an explosion of products marketed directly to the public that claim to address tooth discoloration. Tooth whitening agents aim to remove stains and discolorations. The success of tooth whitening depends on the type of stain present which can be categorized as extrinsic staining, intrinsic staining and internalized discoloration (1). So called "tooth whitening" is a term widely used to describe a change in tooth shade in OTC products marketed to the public. However, the term "tooth whitening" really only describing the end result, while "bleaching" is actually the action that changes the shade of the tooth internally and externally. As OTC products are commonly referred to as "tooth whitening" this term is generically used to describe a change in the tooth shade and the term "tooth whitening agents" refers to the whitening product.

These OTC tooth whitening techniques and materials can easily be applied at-home by the patient. The main difference between at-home teeth whitening and that which are provided / done at the dental practice (in-office) is that at-home tooth whitening involves the patient solely purchasing an OTC whitening agent and applying it independently. Another defining difference between OTC whitening and

in-office is that the patient makes their own diagnosis and decides on which tooth whitening agent/s to use without any diagnosis of the discoloration (2). In numerous countries another factor is the concentration of hydrogen peroxide or carbamide peroxide (1). The percentage of bleaching agent dictates whether it can be sold direct to the public or not. The amount of hydrogen peroxide or carbamide peroxide available to the public varies depending on the country and the respective regulating authority. Therefore, dentist prescribed tray-based bleaching applied at home and in-office bleaching studies and studies that demonstrated whitening products to participants were excluded from this review.

There are numerous tooth whitening products available, such as, dentifrices, mouth rinses, strips, whitening dental floss, toothbrushes, and paint-on gels or film activated charcoal, oil pulling, etc. However, this review focuses on four major categories of OTC whitening agents, whitening dentifrices, whitening strips, whitening mouth rinses and paint of gels / vanishes. Whitening dentifrice is the most common type of OTC tooth whitening agent found, which contains abrasives for stain removal in conjunction with low amounts of hydrogen peroxide and carbamide peroxide (3). Whitening strips were developed mainly to avoid using customized trays and to allow direct utilization from the public. They typically contain hydrogen peroxide ranging from 5-14%, which is applied to teeth, and the active ingredients are released

between 5–60 min once or twice daily (4). Whitening mouth rinses typically contain low concentrations of hydrogen peroxide (1.5%) and sodium hexametaphosphate (4). Paint-on gels or varnishes contain either hydrogen peroxide or carbamide peroxide that adheres to the tooth enamel, and is applied via an applicator onto the tooth surface (5).

There have been reviews that have looked at in office whitening agents and techniques. The last systematic review in 2006 on at-home bleaching products found that all the agents in comparison to placebo/no treatment demonstrated effectiveness. However, the studies included in that review focused only on 2 OTC agents (paint-on gels, and whitening strips) (6). This review investigates the effectiveness of the four major OTC tooth-whitening agents available today. This will be of value to dental practitioners, and will also be informative for the general public.

## Material and Methods

This review was performed in accordance with the PICO approach (Patient or Population, Intervention, Control or Comparison, Outcome, and Study types). The PICO question was formulated as follows: Patient population (P) = General Public, Intervention (I) = Efficacy of OTC agents, Comparison (C) = Efficacy to be compared to dentist prescribed gels, Outcomes (O) = Individual agents efficacy.

A review of the literature published on OTC tooth whitening agents from 2006 until September 2018 was conducted. A search was carried out within Medline (Ovid), PubMed, the Cochrane Library and Cochrane Central Register of Controlled Trials databases. Initially Medline was used to search for articles and a further search in the other databases was used to capture articles not discovered in Medline.

The key words used in Medline (OVID) database were as follows: bleach, bleaching products, tooth, teeth, at home, over the counter, non-prescription, whitening, effects, efficacy, effectiveness, toothpastes, strips, mouth rinses, paint on films, dentifrices, bleaching. The key words were also searched in multiple combinations. The key words used in PubMed database were as follows: over the counter OR at home OR non-prescribed AND efficiency OR effectiveness AND tooth bleaching OR teeth bleaching OR tooth whitening OR teeth whitening. The key words used in Cochrane Library and Cochrane Central Register of Controlled Trials database were as follows: bleach OR bleaching products OR whitening OR toothpastes OR dentifrices OR strips OR mouth rinse OR paint on AND at home OR over the counter AND tooth OR teeth.

The following inclusion and exclusion criteria aimed to include clinical studies done with OTC tooth whitening agents including both chemical and mechanical based agents. Therefore, this review was not confined to randomized controlled clinical studies only. The criteria were made to reflect the whitening agents that are readily available

over the counter without any professional guidance. The inclusion criteria included all clinical studies involving OTC tooth whitening agents (dentifrices, whitening strips, mouth rinses, and paint-on gels/varnishes) from 2006 to September 2018. Studies comparing whitening agents to a placebo or comparing to other whitening agents were also included. Studies that had adults aged 18 years and over were included as they would be the population choosing such agents and applying it independently. The exclusion criteria included studies involving participants of younger than 18 years of age and non-English studies. Dentist prescribed tray-based bleaching kits applied at home and in-office bleaching studies and studies that demonstrated whitening products to participants were excluded. In-vitro studies were excluded as this review aims to provide evidence for making clinical decisions. Whitening chewing gum essentially contain sodium hexametaphosphate (4.0–7.5%) and are promoted to prevent extrinsic tooth stain formation (6), as they are predominately reported to be associated with preventing stain formation they have not been included in the review.

Eight hundred and twelve studies between 2006 and September 2018 were initially identified by the above search parameters. According to the titles, 118 studies were identified as relevant and abstracts retrieved for evaluation. Full text articles were retrieved when further information was required to determine suitability of the study for inclusion. Inclusion and exclusion criteria were applied, which resulted in 24 studies being identified for the final review (Fig. 1).

To identify all information relevant to this review study, the principal researcher followed a two-stage literature search strategy. First, an intensive electronic search of English-language literature published between January 1, 2006, and September 30, 2018. One reviewer verified the eligibility of the potentially relevant articles and independently screened titles and abstracts to evaluate the articles for full-text reading. When the abstract was deficient, titles were used to obtain full texts, and consensus was achieved after discussion with another reviewer. If they disagreed a third reviewer was consulted. In the second round of the search, only studies meeting specific inclusion criteria were selected. Finally, to supplement the electronic search, a hand search was conducted by considering entries in the reference lists of the selected articles, and articles not yet included were then added.

The studies were classified based on the type of tooth whitening agents being trialed such as dentifrices, whitening strips, mouth rinses, and paint-on gels/varnishes. A category was added that grouped all the clinical studies that looked at one or more OTC tooth-whitening agent being trialed. Studies selected were either trialed in comparison with a placebo, no treatment, and dentist-prescribed tray-based gels or with other OTC tooth whitening agents. After the classification into different groups of agents, analysis of full text articles

was carried out by looking into detail at the aim of the study and the methodology carried. The studies were ranked using the GRADE system (British Medical Journal clinical evidence for assessing the quality of studies) to assess the risk of bias (7,8). Studies that were ranked with a score of 3 and above were classified as good quality. Whilst ranking the studies, the critical areas in methodology such as randomization, blinding, process of inclusion of participants, preparation of participants or specimens, consistency in process of shade taking before and after tooth whitening procedures, determined the GRADE ranking. Results and conclusion of each study were reported. After identifying each of the categories above and ranking each study, good quality studies were further reviewed to ascertain the effectiveness of the tooth whitening agents investigated. To determine the effectiveness of each agent all of the included studies' conclusions were considered, along with the quality of the studies, with the higher quality studies ultimately being the main contributing factor. The present study was conducted and reported adhering to the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) statement (9).

## Results

From the 24 studies included in this review, 22 randomized clinical studies, 1 was a randomized double-blind study, and 1 was a clinical study. Ten studies were on whitening dentifrices, 7 on whitening strip, and 2 on paint-on gels/varnish. No in vivo studies were identified relating to the whitening mouth rinses. Five studies compared two or more OTC agents (Boxes 1-3).

With regards to shade analysis, 11 studies used digital

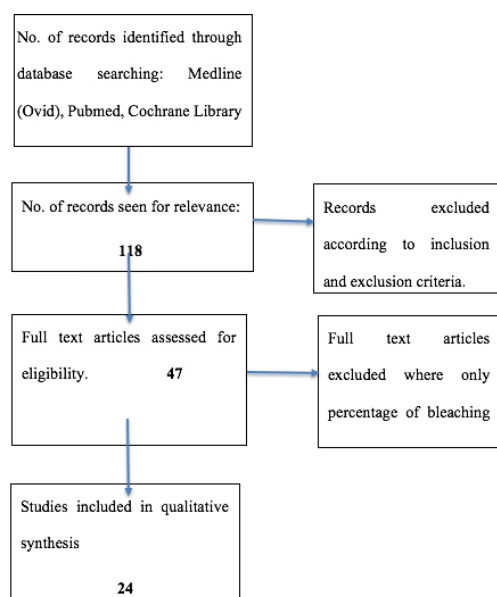


Figure 1. Process of identifying studies.

imaging, 1 used digital imaging in conjunction with a shade guide and 1 used digital imaging in conjunction with the WIO: Whiteness formula index. Five studies used a VITA Classic shade guide and 5 used the Lobene Stain Index or a Modified Lobene Stain Index (Boxes 1-4). The studies observational periods were not consistent with only one study having a period more than a year. The age range of participants was from 18 to 77.

The largest numbers of studies were related to whitening dentifrice, which included 8 randomized clinical study, 1 randomized double-blind clinical study, 1 controlled crossover clinical study, and 1 clinical study (Box 1). The tooth whitening elements varied considerably amongst studies. Tooth whitening protocols involved brushing from 1 to 3 min twice daily. The quality of the studies ranged from GRADE 0-3, with 2 studies of good quality reporting that dentifrice was effective in changing the shade of the tooth (via stain removal) (Box 1) (10,11), but had lower effectiveness when compared to whitening strip as shown in Box 4 (12).

There were 2 good quality studies that investigated whitening strips, which determined that whitening strips were effective (Box 2) (13,14), and were also effective when compared to other tooth whitening agents (12,15-17). There were 7 studies on whitening strips included, all 7 were randomized clinical studies (Box 2). The sample size was below 50 in all these studies and all the studies reported significant change. The main whitening agent used was hydrogen peroxide with concentration ranging from 5 to 10%. The application protocol was twice daily for 30 min, which varied from 14 days to 6 weeks.

There were no good quality studies in relation to paint-on gels, as shown in Box 3. However, in Box 4, there are 3 good quality studies that compared paint-on gels with whitening strips and all reported that whitening strips were more effective than paint-on gels (15,17,18). There were 2 studies that trailed paint-on gels/varnishes; these were randomized clinical studies and both had a GRADE 2 (Box 3) (19,20). The main whitening agent used for paint-on gels/varnish was hydrogen peroxide, which was in different concentrations in the studies. Paint-on agents were of a gel or varnish medium. The protocols differed between the two studies, ranging from the varnish being applied for 10 min for 5 days to the gel being applied for 15 min for 14 days.

Five studies compared two or more OTC whitening agents (Box 4). There were 4 randomized clinical studies and 1 clinical study. There were different agents with different tooth whitening protocols. The quality ranged was predominantly good, with 4 out of the 5 studies having a GRADE score of 3. All studies that included whitening strips, determined that whitening strips were more effective than the other OTC whitening agents, such as dentifrices and paint-on-gels.

Box 1. Description of whitening dentifrice clinical studies

Authors	Study design	n	Whitening agent	Whitening protocol	Shade appraisal
Collins et al., 2008	Controlled cross-over clinical study	78	Group 1: Blue covarine Group 2: Placebo (Clear gel)	Group 1 Brush for 1.5 min twice daily for 1 day Group 2: Brush for 1.5 min twice daily for one day	S WIO Index
Forner et al., 2012	Clinical study	20	5% lactoperoxidase + 3% carbamide peroxide Group 1: 35% sodium bicarbonate, sodium fluoride, Amorphous calcium phosphate (Truly radiant toothpaste)	Brush for 3-4min 3 times daily for 21 days Group 1: Brush for 2 min twice daily for 6 weeks	S
Ghassemi, 2015	Randomized controlled study	178	Group 2: Crest 3D whitening toothpaste (positive control) Group 3: Colgate cavity protection (negative control)	Group 2: Brush for 2 min twice daily for 6 weeks Group 3: Brush for 2 min twice daily for 6 weeks	VCS
Ghassemi, 2012	Randomized controlled study	135	Group 1: Sodium bicarbonate Group 2: Placebo (silica based)	Group 1: Brush for 1 min twice daily for 6 weeks Group 2: Brush for 1 min twice daily for 6 weeks	VCS
Ghassemi et al., 2015	Randomized controlled study	54	Group 1: 20% sodium bicarbonate, sodium fluoride, tetrasodium pyrophosphate (Truly Radiant Rejuvenating toothpaste) Group 2: Colgate cavity protection (negative control)	Group 1: Brush for 2 min twice daily for 5 days Group 2: Brush for 2 min twice daily for 5 days	LSI
Horn et al., 2014	Randomized clinical study	60	Group 1: Water, hydrated silica, sodium lauryl sulphate, sodium hydroxide, sodium fluoride, Triclosan, sodium saccharin, titanium dioxide (Colgate Total 12) Group 2: Water, sorbitol, hydrated silica, sodium lauryl sulphate, sodium fluoride, sodium saccharin, trisodium phosphate, dipentene (Close Up White Now) Group 3: Sodium fluoride, water, hydrated silica, sorbitol, sodium lauryl sulphate, sodium hydroxide, sodium saccharin (Oral B 3D White) Group 4: Water, hydrated silica, sorbitol, pentasodium triphosphate, tetrapotassium pyrophosphate, sodium lauryl sulfate, polyethylene, cocamidopropyl betaine, sodium saccharin, sodium hydroxide, sodium fluoride, titanium dioxide, blue #1 aluminium lac (Colgate Luminous White)	Groups 1- 4: Brush for 2-3 min, 3 times daily for 15 days	S
Nathoo et al., 2008	Randomized clinical study	Study 1: 114 Study 2: 119	Studies 1 and 2 Group 1: 0.3% triclosan/ 2.0% PVM/MA copolymer/0.243% sodium fluoride in a 17% dual silica base (Colgate Total Advanced) Group 2: 0.243% sodium fluoride in a silica base (Crest Cavity Protection)	Studies 1 and 2 Group 1: Brush for 1min twice daily for 6 weeks Group 2: Brush for 1min twice daily for 6 weeks	LSI

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Baseline	Shade change x days after treatment						GRADE score
	0 days	5 days	2 weeks	3 weeks	6 weeks	8 weeks	
Group 1 WIO: -55.28 (1.70)	Group 1 ΔWIO: 1.14 (0.30) (p<0.05)						0
Group 2: WIO: -55.03(1.71)	Group 2: ΔWIO: 0.08 (0.31)						
Shade B2 or darker				ΔE:5.14			0
Group 1: VCS: 8.981 (2.57)					Group 1: ΔVCS: -2.08 (p<0.05)		
Group 2: VCS: 8.969 (2.39)					Group 2: ΔVCS: -1.467 (p<0.05)		0
Group 3: VCS: 9.079 (2.78)					Group 3: ΔVCS: - 0.038 (p=0.6713)		
Group 1: VCS: 9.77 (2.26)					Group 1: ΔVCS: -2.57 (0.99)		1
Group 2: VCS: 9.17 (2.14)					Group 2: ΔVCS: -0.04 (0.69)		
Group 1: LSI: 3.094 (0.99)		Group 1: ΔLSI: 2.38 (0.99)					2
Group 2: LSI: 3.273 (1.79)		Group 2: ΔLSI: 3.32 (1.80)					
Group 1: L: 82.9			Group 1: ΔE: -0.25				
Group 2: L: 83.9			Group 2: ΔE: -0.48				
Group 3: L: 83.9			Group 3: ΔE: 0.29				1
Group 4: L: 86.4			Group 4: ΔE: 1.15				
Study 1 Group 1: LSI: 0.68 ± 0.21					Study 1 Group 1: ΔLSI: - 0.12 ± 0.11		
Group 2: LSI 0.70 ± 0.17					Group 2: ΔLSI: 0.25 ± 0.16		0
Study 2 Group 1: LSI: 1.30 ± 0.25					Study 2 Group 1: ΔLSI :- 0.79 ± 0.36		
Group 2: LSI: 1.6 ± 0.23					Group 2: ΔLSI: -1.52 ±0.48		

Over-the-counter tooth whitening agents

Authors	Study design	n	Whitening agent	Whitening protocol	Shade appraisal
Raoufi, Birkhed, 2010	Randomised double blind clinical study	15	Group 1: Hydroxyapatite, hydrated silica, potassium nitrate, fluoride. Group 2: Calcium peroxide, hydrated silica, fluoride Group 3: Toothpaste C: hydrated silica, fluoride (no active ingredient)	Group 1: Brush for 2 min twice daily for 12 weeks Group 2: Brush for 2 min twice daily for 12 weeks Group 3: Brush for 2 min twice daily for 12 weeks	S & VCS
Terezhalmly et al., 2007	Randomized controlled study	Study 1: 29 Study 2: 30	Studies 1 and 2 Group 1: Stannous fluoride sodium hexametaphosphate (Crest Prohealth) Group 2: Positive control group (Colgate total + whitening)	Studies 1 and 2 Group 1: Brush dentifrice for 1 min twice daily for 2 weeks Group 2: Brush dentifrice for 1 min twice daily for 2 week	MLSI
A. S. Naidu et al. Terezhalmly et al., 2007	Randomized clinical study	Study 1: 21 Study 2:30	Study 1 / Group1: Sodium fluoride/sodium hexametaphosphate (Crest Vivid White) + manual toothbrush Group 2: Crest Cavity protection + powered toothbrush Study 2 / Group 1: Sodium fluoride/sodium hexametaphosphate (Crest Vivid White Night + Crest cavity protection) + manual toothbrush Group 2: Cavity protection dentifrice + powered toothbrush	Study 1 Both groups Brush twice daily for 2min for 2 weeks Study 2 Group 1: Brush with Crest Vivid White Night at night for 2 min and Cavity protection in the morning for 2 min Group 2: Brush twice daily for 2min for 2 weeks	LSI
Young et al., 2015	Randomized clinical study	133	Group 1: 5% sodium tripolyphosphate, 5% potassium nitrate, 1150 ppm fluoride as NaF (ultra-low abrasivity) Group 2: 5% sodium tripolyphosphate, 5% potassium nitrate, 1% alumina, 1150 ppm fluoride as NaF (low abrasivity) Group 3: A standard fluoride dentifrice: 923ppm NaF (moderate abrasivity) Group 4: Daily use whitening dentifrice: 1100ppm NaF (high abrasivity)	Brush for 1 min twice daily for 8 weeks	MLSI

Baseline	Shade change x days after treatment						GRADE score
	0 days	5 days	2 weeks	3 weeks	6 weeks	8 weeks	
Group 1: VCS: 38.2					Group 1: ΔVCS: 37.7		
Group 2: VCS: 40.7					Group 2: ΔVCS: 41.2		1
Group 3: VCS: 39.5					Group 3: ΔVCS: 40.0		
Study 1 Group 1: MLSI: 1.56			Study 1 Group 1: MLSI: 0.95				
Group 2: MLSI: 1.65			Group 2: MLSI: 0.94				3
Study 2 Group 1: MLSI: 2.95			Study 2 Group 1: MLSI: 2.61				
Group 2: MLSI: 2.64			Group 2: MLSI: 2.60				
Study 1 Group 1: LSI: 2.09			Study 1 Group 1: ΔLSI: 1.84				
Group 2: LSI: 2.49			Group 2: ΔLSI: -2.20				1
Study 2 Group 1: LSI: 2.71			Study 2 Group 1: ΔLSI: 2.31				
Group 2: LSI: 2.76			Group 2: ΔLSI: -2.38				
MLSI: score ≥ 45					Group 1: ΔMLSI: -0.48 (0.03)		
					Group 2: ΔMLSI: -0.53 (0.03)		3
					Group 3: ΔMLSI: -0.51 (0.03)		
					Group 4: ΔMLSI: -0.55 (0.03)		

NaF: Sodium fluoride. WIO: *Whiteness* formula index. VCS: Vitapan Classical Shade Guide. LSI: \*Lobene Stain Index. S: Spectrophotometer. MLSI: Modified Lobene Stain Index. L: Lightness. ΔWIO: Changes in whiteness of teeth according to WIO index. ΔVCS: Change in tooth shade according to VCS. ΔLSI: Change in tooth shade according to LSI. ΔE: Color difference before and after treatment according to S. ΔMLSI: Change in tooth shade according to MLSI.

*Lobene Stain Index Score	Intensity Description	Area Description
0	No Stain	No Stain
1	Light Stain (yellow to light brown or grey)	Stain covering up to 1/3 of the region
2	Moderate Stain (medium brown)	Stain covering 1/3 up to 2/3 of the region
3	Heavy Stain (dark brown to black)	Stain covering > 2/3 of the region

Box 2. Description of whitening strips clinical studies

Authors	Study Design	n	Whitening Agent	Whitening Protocol	Color Appraisal
Auschill et al., 2012	Randomized clinical study	28	Group 1: 5.3% HP strips	Group 1: Twice daily for 30 min for 2 weeks	VCS
			Group 2: 5.0% HP tray at home	Group 2: Twice daily for 30 min for 2 weeks	
da Costa et al., 2012	Randomized clinical study	24	Group 1: 14% HP strips	Group 1: Twice daily for 30 min for 2 weeks	S
			Group 2: 35% CP tray at home	Group 2: Twice daily for 30 min for 2 weeks	
Ferrari et al., 2007	Randomized clinical study	36	Group 1: 6% HP strip	Group 1: Twice daily for 30 min for 2 weeks	S
			Group 2: 10% CP tray at home	Group 2: Twice daily for 30 min for 2 weeks	
Hanning et al., 2007	Randomized clinical study	47	Group 1: 6% HP strips	Group 1: Twice daily for 30 min for 2 weeks	S
			Group 2: 10% CP tray at home	Group 2: 1 hr daily for 2 weeks	
Guerrero et al., 2007	Randomized controlled study	30	Group 1: 6.5% HP strips	Group 1: Twice daily for 30 min for 3 weeks	S
			Group 2: Placebo	Group 2: Twice daily for 30 min for 3 weeks	
Oliveira et al., 2013	Randomized clinical study	39	Group 1: 9.5% HP strips	Group 1: 2 hrs daily for 9 days	S
			Group 2: 10% HP strips	Group 2: 30 min daily for 9 days	
Swift et al., 2009	Randomized controlled study	35	Group 1: 6% HP strips	Group 1: Twice daily for 30 min for 6 weeks	S
			Group 2: Placebo strips (no HP)	Group 2: Twice daily for 30 min for 6 weeks	

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	Shade change x days after treatment						GRADE score
	Baseline	9 days	3 weeks	4 weeks	6 weeks	18 months	
Shade A <sub>3</sub> or darker Group 1: VCS=9.68±0.95						Group 1: VCS= -6.35±3.5 shades	2
						Group 2: VCS= -6.41 ± 2.65 shades	
Group 1 & 2: Equal or darker than 1M2 Master VITA bleach guide				Group1:ΔE:6.5			1
						Group2: ΔE:7.5	
Group 1: L: 75.0 (2.46)					Adjusted mean Group1: ΔL: 1.20 (0.24)		1
Group 2: L: 74.1 (2.15)					Group2: ΔL: 0.90 (0.23)		
Group 1: L: 73.55±1.83					Group 1: ΔL: 1.55 ±0.41		1
Group 2: L: 73.22±1.59					Group 2: ΔL:1.20±0.37		
Group 1: W: 32.0 (1.69)				Group 1: ΔW:4.76 (0.27)			2
Group 2: W: 31.8 (1.36)				Group 2: ΔW:0.21 (0.28)			
Group 1 & 2: Shade A <sub>2</sub> or darker. L: 65.2-74.1		Group1: ΔE:3.8 (0.3) (p<0.05)					3
		Group2: ΔE*:2.3 (0.3) (p<0.05)					
Group 1 & 2: L: 68.0-76.8					Group 1: ΔE: 4.6 (0.3) (p<0.05)		3
					Group 2: ΔE: 1.0 (0.3) (p<0.05)		

HP: Hydrogen peroxide; CP: Carbamide peroxide; S: Spectrophotometer; ΔE: Color difference before and after treatment according to S  
L: Lightness; ΔL: Lightness difference before and after treatment according to S; VCS: Vitapan Classical Shade Guide; VCS: Change in tooth shade according to VCS; W: Whiteness; ΔW: Change in the closeness to white.

## Discussion

This review attempts to determine the effectiveness of major OTC tooth whitening agents currently available. It was challenging to analyze the effectiveness of a particular whitening agent compared to another due to the lack of consistent research protocols. For example, some studies dried the teeth after tooth whitening to assess the shade and others did not or did not specify. This was again inconsistent with regards polishing of teeth and the positioning shade taking device on the arch was specified in some studies, and not others. The temperature of the light source in the room were often not clear and which teeth were measured to assess the bleaching efficiency was often not identified. Also, the color-measuring instrument are not consistent with some studies using conventional color measuring techniques, while others used digital directly or indirectly. Spectrophotometers can determine a color change that cannot be perceived by the human eye; however, it is challenging to take multiple measurements when removing the instrument from the tooth as placing the instrument back in the same location is critical to having consistent readings. Multiple studies used a shade assessment technique/device that were only suitable to determine the change in the surface shade, for example the Lobene stain index measures surface stain removal of only, and not change in tooth color.

In this review, 10 studies used subjective measures (Vita Classic shade guide, Lobene Stain Index and modified Lobene Stain Index), 14 used an objective device (spectrophotometer) and only 1 study used both type of

these measures. A review stated that spectrophotometer provides a more consistent comparison of shade change as opposed to conventional shade guides. Conventional shade guides allow a non-linear evaluation of a specific shade without considering hue, value and chroma separately. Specific shade guides such as the Vita 3D Master or digital imaging devices provide a linear evaluation of a shade considering its hue, value, and chroma separately. This highlights an important point when analyzing the results, as different tools would give different levels of accuracy of shade. This brings into question the accuracy of shade measurements and the results of studies that used a VITA Classic shade guide. It has been recommended that the best way to ensure precise shade taking is to use both subjective and objective measures (21).

It could be argued that all OTC studies have an element of bias due to the studies evaluation process and the inclusion and exclusion criterion being applied. An area of possible bias is that a number of studies involved researchers that were employees of the whitening agent manufacturer and the majority of the studies involving whitening strips and dentifrices were either partially or fully funded by the manufacturers. Not every study had standardized patient selection (age, hygiene, baseline color, and diet). Several studies provided instructions or demonstrated how to apply the OTC whitening agent, which could skew the outcomes, as OTC products are provided with no professional advice.

### Whitening Dentifrices

Whitening dentifrices is one of the OTC agents that are

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Box 3. Description of paint-on gel / varnish clinical studies

Authors	Study design	n	Whitening agent	Whitening protocol	Color appraisal	Shade change x days after treatment			GRADE score
						0 day	14 days	6 months	
Oteo Calatayud et al., 2009	Randomized clinical study	16	Group 1: 6% HP varnish in office	Group 1: 5 applications per session per week for 2 weeks	VCS	A2 or darker	Group 1: VCS: -2.8 shades (p<0.05)		2
			Group 2: 6% HP varnish at-home	Group 2: Once daily 10 min for 10 days			Group 2: VCS: -2.5 shades (p<0.05)		
Zantner et al., 2006	Randomized clinical study	60	Group 1: 5.9% HP paint-on	Group 1: 15 min twice daily for 2 weeks	VCS	A2 or darker	Group 1: VCS: - 0.64 (±2.18) shades (p<0.05)		2
			Group 2: Sodium Chlorite tray	Group 2: 10 min once daily for 2 weeks			Group 2: VCS: -0.40 (±1.46) shades		

HP: Hydrogen peroxide. VCS: Vitapan Classical Shade Guide. ΔVCS: Change in tooth shade according to VCS.

easily available to the public and low-cost. Three studies were of good quality and the remaining 7 were of lower quality (GRADE from 0 to 1). Many of the clinical studies used randomization and there was a mix of double blinded and single blinded studies. There were no set whitening or abrasive components, with some containing, baking soda, papain, hydroxyapatite, calcium carbonate and sodium fluoride. Two studies were identified that had blue covarine as a tooth-whitening agent. Blue covarine is a pigment that is uniformly deposited and retained on pellicle coated tooth surfaces. It is claimed to cause a color shift from yellow to blue, creating an illusion of tooth whitening (22,23). These studies were not included in the review, as blue covarine does not remove stains or break down pigments and it merely adds a layer to create a lightening effect.

Some studies stated that the new dentifrices containing baking soda, peroxide, amorphous calcium phosphate ("active calcium") and tetrasodium pyrophosphate were effective whitening agents (24–26). Experimental dentifrices claimed to have some effectiveness with new contents such as in enzymatic dentifrices containing lactoperoxidase and carbamide peroxide (27), dual silica system and dentifrices containing sodium hexametaphosphate (10,28,29). However, objective measurements did not show effectiveness in a trial carried out with hydroxyapatite and calcium peroxide for removal of extrinsic stains (30).

There was one lower quality study that reported that whitening dentifrices were not effective in changing tooth shade (31). There were 2 studies of good quality that determined that dentifrices are effective "by removing extrinsic stains" in comparison to a placebo. When dentifrices are compared to tooth whitening strips (Box 4), their effectiveness is not comparable. Yudhira et al, compared whitening dentifrice to whitening strips and determined that significant changes were seen in the strip group, but not with the dentifrice group (12).

### *Whitening Strips*

In this review, 7 studies looked into whitening strips comparing them with either a placebo, carbamide peroxide tray, or whitening strips of different concentration. Five studies were randomized clinical studies, and five studies used hydrogen peroxide concentration in the range of 5 to 6.5% and the 2 remaining studies used high concentrations of hydrogen peroxide (9.5–14%). The length of the studies varied from 14 days to 18 months with a standard exposure time of 30 min twice daily in all studies (Box 2). The shade taking environments were not well described and the usage of color correction lights was not specified in most studies. There was inconsistency in the studies with some not providing adequate details of the shade taking protocols. The majority of studies used a spectrophotometer.

Two studies showed that whitening strips versus placebo strips produced a significant improvement in shade (14,32). Four studies reported that strips were effective and comparable to carbamide peroxide tray treatment (33–36). One study reported that whitening strip at 6% hydrogen peroxide showed superior effectiveness compared to 10% carbamide peroxide in gel tray treatment (33). A similar result was seen in a previous review that reported that strips at 6% hydrogen peroxide were more effective than 10% carbamide peroxide (6). It is interesting to note that the 2 studies that used whitening strips with 6% hydrogen peroxide and 10% carbamide peroxide used an application protocol of 30 min twice a day. This is not the typical application protocol for carbamide peroxide which is typically 2–4 h per day or overnight (35,36). This would most likely severely affect the ability of the carbamide peroxide products performance. A systematic review and meta-analysis reported that there was no significant difference between whitening strips and 10% carbamide peroxide gel whitening treatment regime (37). Furthermore, a systematic review by Luque-Martinez determined that carbamide peroxide tray treatment showed slightly better efficacy compared to whitening strips (38).

Two good quality studies showed that whitening strips were effective and that increased exposure time gave better results (13,14). Oliveira et al. (13) determined that a lower hydrogen peroxide concentration on strip with an extended application time showed better effectiveness than a strip with a higher hydrogen peroxide concentration applied for a shorter time. This is an interesting observation and illustrates the rate at which the peroxide is released is a factor to consider. Carbamide peroxide tray gels are slow release whereby only 50% of its peroxide is released in the first 2–4hrs and the rest over 2–6hrs, hence allowing better oxidation of the organic matrix (38). Therefore, the peroxide concentration and release rate are essential, as well as the duration of exposure (36). When compared to other OTC tooth whitening agents (Box 4), whitening strips have been seen to be effective in the majority of the studies.

### *Paint-on Varnish/Gels*

There were only 2 studies included in this category of tooth whitening agent. Both were randomized clinical studies and used Vita Classic shade guides. Both studies concluded to varying degrees that paint-on gels were an effective means of tooth whitening (6,18). Oteo Calatayud et al. (18) also concluded that there was no difference in the effectiveness if the application of paint-on varnish when done at home or in an office. While effective changes were reported by Oteo Calatayud et al. (18), Zantner et al. (20) found was little shade change after 6 months. The result was attributed to the fact that patients were advised to close

their mouth immediately after application as per directed by the manufacturer's instructions. It pointed out that previous studies that had shown effectiveness allowed 30 s for the gel to dry before closing. A systematic review (6) stated paint-on gels applied three times a day were more effective than twice daily. This study (6) also stated that

paint-on gels at a higher percentage of hydrogen peroxide were more effective than lower percentage gels, which is contradictory to the results of Oteo Calatayud et al. (18). Although Oteo Calatayud et al. (18) reported effectiveness of paint-on gels, it is difficult to declare paint-on gels as effective based on the limited evidence.

Box 4. Description of clinical studies that compared two or more OTC whitening agents

Authors	Study design	n	Whitening agent	Whitening protocol	Shade appraisal	
A. S. Naidu et al.	Bizhang et al., 2007	71	Group 1: 6% HP whitening strips	Group 1: 30 min twice daily for 2 weeks	S	
			Group 2: 19% sodium percarbonate brush applied gel	Group 2: 1 Brush application daily for 14 nights		
			Group 3: Placebo without peroxide	Group 3: 1 Brush application daily for 14 nights		
	Bizhang et al., 2009	Clinical study	75	Group 1: 6% HP whitening strips	Group 1: 30 min twice daily for 2 weeks	S
				Group 2: 10% CP tray at home	Group 2: Overnight for 2 week	
				Group 3: 15% HP in office	Group 3: 45 min once daily, 3 times for 3 weeks	
Lo et al., 2007	Randomized controlled study	63	Group 1: 6% HP whitening strips	Group 1: 30 min twice daily for 2 weeks	S	
			Group 2: 18% CP paint-on gel	Group 2: 15 min twice daily for 2 weeks		
			Group 3: Placebo (strips and 6% Fluoride)	Group 3: 30 min twice daily for 2 weeks		
Yudhira et al., 2007	Randomized controlled study	46	Group 1: 6% HP whitening strips	Group 1: 30 min twice daily for 2 weeks	S	
			Group 2: Whitening toothpaste NaF	Group 2: Twice daily for 12 weeks		
			Group 3: Whitening toothpaste MFP	Group 3: Twice daily for 12 weeks		
Xu Xiao et al., 2007	Randomized controlled study	49	Group 1: 6% HP whitening strips	Group 1: Twice daily for 1 week	S	
			Group 2: 5.9% HP paint-on gel	Group 2: Twice daily for 2 weeks		
			Group 3: Placebo (water rinse)	Group 3: Twice daily for 2 weeks		

### Comparison of Different Over-The-Counter Tooth Whitening Agents

In this review several studies compared two or more OTC tooth whitening agents allowing comparison. There were 5 studies included in this category, out of which 4 were of good quality (Box 4) which reported the superior

effectiveness of whitening strip compared to other OTC tooth whitening agents (12,15,17,18).

In general whitening strips showed superior effectiveness when compared to other OTC tooth whitening agents such as mouth rinses, dentifrices and paint-on gels. This was contributed to the higher contact time and the

	Shade change x days after treatment						GRADE score
	Baseline	15 days	6 weeks	12 weeks	3 months	6 months	
VCS:A2 or darker						Group 1: $\Delta L$ : 2.37 (0.11) Group 2: $\Delta L$ : 1.46 (0.12) Group 3: $\Delta L$ : 0.20 (0.11)	3
VCS:A2 or darker					Group 1: $\Delta E$ : 2.99 (1.39) Group 2: $\Delta E$ : 4.59 (1.42) Group 3: $\Delta E$ : 3.58 (1.57)		1
VCS:A2 or darker			Group 1: $\Delta L$ : 2.5 (0.27) Group 2: $\Delta L$ : 0.6 (0.19) Group 3: $\Delta L$ : 0.1(0.22)				3
Group 1: L: 75.90 (1.15) Group 2: L: 75.49 (0.99) Group 3: L: 75.51 (2.13)				Group 1: $\Delta L$ : 2.36 (0.24) Group 2: $\Delta L$ : 0.15 (0.24) Group 3: $\Delta L$ : 0.45 (0.24)			3
Group 1: L: 75.06 (1.98) Group 2: L: 75.11 (1.29) Group 3: L: 75.06 (1.76)	Group 1: $\Delta L$ : 1.88 (0.21) Group 2: $\Delta L$ : 0.60 (0.15) Group 3: $\Delta L$ : -0.10 (0.18)						3

HP: Hydrogen peroxide. CP: Carbamide peroxide. NaF: Sodium fluoride. MFP: Mono-fluorophosphate. VCS: Vitapan Classical Shade Guide. S: Spectrophotometer.  $\Delta E$ : Color difference before and after treatment according to S.  $\Delta L$ : Lightness difference before and after treatment according to S.

concentration of hydrogen peroxide of whitening strips. The difference between paint-on gels and whitening strips effectiveness is attributed to the fact that the strip acts as a fixed barrier (reservoir) unlike paint-on gels (15). All studies were randomized according to age and the color of teeth. From this review it could be concluded that when comparing with OTC tooth whitening agents, whitening strips have consistently been proven to have superior effectiveness.

Within the limitations of this study and from the evidence, it can be concluded that with regards to the effectiveness of OTC tooth whitening agents:

Whitening strips are an effective OTC tooth-whitening agent when compared to a placebo, other OTC tooth whitening agents, however their effectiveness compared to tray-based gels with carbamide peroxide is debatable and dependent on the carbamide peroxide percentage and the application timespan.

Whitening dentifrices are effective in changing the shade of the tooth "by removing extrinsic stains" when compared to a placebo and non-whitening dentifrices. They are not as effective when compared with tooth whitening strips.

3. There is a lack of evidence to make a conclusion with regards the effectiveness of paint-on gels whitening agents.

There is a need for more independent standardized clinical studies and randomized clinical studies in the area of OTC products effectiveness.

The majority of the studies were conducted over a short time span, which may not represent the true effectiveness of the product tested. The aspect of relapse therefore would be an area for further research.

## Resumo

Há um aumento da acessibilidade dos agentes clareadores de venda livre com poucos dados na literatura sobre sua eficácia. Esta revisão foi feita para determinar a eficácia dos agentes clareadores de venda livre predominantes de 2006 a 2018, onde foi feita uma comparação de cada agente com um placebo, sem tratamento ou com outros agentes clareadores de venda livre. As principais categorias de agentes clareadores de venda livre, como dentifrícios, tiras branqueadoras e géis. Estudos em que o dentista prescreveu clareamento caseiro e em consultório, e estudos que demonstraram os agentes clareadores para os participantes. Os artigos foram pesquisados nas bases de dados do Medline (Ovid), PubMed, Cochrane Library e Cochrane Central Register of Controlled Trials. Vinte e quatro artigos foram incluídos na revisão sistemática e a qualidade dos estudos foi determinada pelo critério de classificação GRADE (Classificação de Recomendações, Avaliação, Desenvolvimento e Avaliações). Em comparação com outros clareadores de venda livre, as tiras são relatadas como eficazes. Dois estudos determinaram que as tiras de clareamento são eficazes. As tiras de clareamento mostraram-se eficazes quando comparadas com placebos e outros agentes clareadores de venda livre. Os dentifrícios são eficazes na mudança da tonalidade do dente "removendo manchas extrínsecas" quando comparados a dentifrícios com placebo e sem clareamento, mas não são tão eficazes em comparação com as tiras de clareamento. Há uma falta de evidência com relação à eficácia dos géis de tinta. Embora exista alguma evidência

de que os clareadores de venda livre possa alterar a tonalidade no curto prazo, há necessidade de estudos melhor projetados.

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