SYSTEMATIC REVIEW

REVISED Effect of whitening toothpaste on surface roughness and microhardness of human teeth: a systematic review and meta-analysis [version 3; peer review: 2 approved, 1 approved with reservations]

Navodita Jamwal, Ashwini Rao, Ramya Shenoy, Mithun Pai, Aparna KS, Avinash BR

Public Health Dentistry, Manipal College of Dental Sciences, Mangalore, Manipal Academy of Higher Education, Manipal, India, Mangalore, Karnataka, 575001, India

v3 **First published:** 11 Jan 2022, **11**:22
https://doi.org/10.12688/f1000research.76180.1
Second version: 14 Feb 2022, **11**:22
https://doi.org/10.12688/f1000research.76180.2
Latest published: 08 Mar 2022, **11**:22
https://doi.org/10.12688/f1000research.76180.3

Abstract

Background: Whitening toothpastes exert a whitening effect on teeth through higher surface cleaning effectiveness resulting from the abrasive properties of the paste or specific chemical components. This systematic review and meta-analysis was conceptualized to examine the relationship between whitening toothpastes and surface roughness as well as microhardness of human teeth and to clarify the evidence base available around this relationship by conducting a systematic review and meta-analysis of studies in this topic area, looking at *in vitro* randomized control trials.

Methods: Criteria for including studies in the review were done based on population, intervention, comparison, outcomes and study and studies were identified from electronic databases. Covidence® was used for data screening and data extraction. The CONSORT tool was used for checking relevant content and methodology used in each of the papers reviewed. Systematic review was done followed by meta-analysis, using Review Manager.

Results: A total of 125 articles were obtained on key word search. After duplicate removal and title screening, 17 articles were eligible for full text review. Finally, 7 studies were included for systematic review and meta-analysis was conducted on 4 studies. The forest plot for surface roughness showed that that the meta-analytic effect was statistically significant with surface roughness value being higher in the intervention group. The forest plot for microhardness showed that the meta-analytic effect was statistically significant with the microhardness value being lesser in the intervention group.

Open Peer Review

Approval Status ? ✓ ✓

	1	2	3
version 3 (revision) 08 Mar 2022			✓ view
version 2 (revision) 14 Feb 2022		✓ view	
version 1 11 Jan 2022	? view		? view

1. **Dimitrios Dionysopoulos**, Aristotle University of Thessaloniki, Thessaloniki, Greece
2. **Ashish Shrestha**, B. P. Koirala Institute of Health Sciences, Dharan, Nepal
3. **Harsh priya**, All India Institute of Medical Sciences, New Delhi, India

Any reports and responses or comments on the article can be found at the end of the article.

Conclusions: Although whitening toothpastes typically can lighten tooth color by about one or two shades, there is some evidence to show that these toothpastes also affect the mineral content of teeth by increasing surface roughness and reducing microhardness. More evidence and further research are needed to identify the type of whitening agent which will whiten the tooth effectively while maintaining the integrity of the tooth structure.

Keywords
dental enamel, in-vitro study, meta-analysis, micro hardness, surface roughness, systematic review, whitening toothpaste

This article is included in the Manipal Academy of Higher Education gateway.

Corresponding author: Ashwini Rao (ashwini.rao@manipal.edu)

Author roles: Jamwal N: Data Curation, Formal Analysis, Investigation, Methodology, Resources, Software, Validation, Writing – Original Draft Preparation, Writing – Review & Editing; **Rao A**: Conceptualization, Data Curation, Formal Analysis, Methodology, Project Administration, Resources, Software, Supervision, Validation, Visualization, Writing – Review & Editing; **Shenoy R**: Formal Analysis, Software, Validation, Writing – Review & Editing; **Pai M**: Software, Supervision, Visualization, Writing – Review & Editing; **KS A**: Resources, Software, Supervision, Writing – Review & Editing; **BR A**: Resources, Visualization, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

How to cite this article: Jamwal N, Rao A, Shenoy R *et al.* **Effect of whitening toothpaste on surface roughness and microhardness of human teeth: a systematic review and meta-analysis [version 3; peer review: 2 approved, 1 approved with reservations]** F1000Research 2022, **11**:22 https://doi.org/10.12688/f1000research.76180.3

First published: 11 Jan 2022, **11**:22 https://doi.org/10.12688/f1000research.76180.1

REVISED **Amendments from Version 2**

In Table 1, under the characteristics of included studies, Bolay 2012 - 20.000 brush strokes has been corrected to 20,000.

Any further responses from the reviewers can be found at the end of the article

Introduction

"Tooth whitening is a conservative and effective method to lighten discolored teeth and has been practiced in dentistry for many centuries".[1] Management of discolored teeth, was earlier done by tooth whitening material in the form of oxalic acid, chlorine, ammonia and hydrogen peroxide.[2] Whitening of teeth can be done professionally in the dental practice by scaling and polishing, bleaching or by using prosthetic crowns; it can also be done at home, by the individual themselves, using an over the counter whitening toothpaste.[1] The role of a whitening toothpaste is to remove unwanted surface deposits and stains with minimal effect on the tooth structure.[3]

Whitening toothpastes exert their action either because of the abrasive properties of the paste or because of specific chemical components, such as silica, aluminum oxide, sodium bicarbonate, carbamide peroxide and hydrogen peroxide or a combination of these.[4] Although all toothpastes contain abrasives, whitening toothpastes often contain a higher amount of harder abrasives.[5] Bleaching compounds like calcium and magnesium peroxide and sodium percarbonate have also been used in whitening toothpastes. Other whitening agents that have been used are surfactants, colorants, enzymes and polyaspartate.[6,7] Presently some toothpastes have also started using activated charcoal as a whitening agent because it has the capacity of adsorbing pigments and stains.[1] Studies have shown that whitening toothpastes can bring about changes to the surface roughness and microhardness of teeth.[8,9]

Rationale

The extraordinary mechanical properties of a tooth with respect to hardness and fracture toughness is due to the chemical and structural interaction between the inorganic hydroxyapatite and the organic protein matrix.[1] Studies have reported structural damage to enamel surface prisms and increased tooth sensitivity during professional teeth whitening in the dental clinic.[10–12] However, conflicting results have been reported with respect to the clinical efficiency of home use whitening toothpastes, with many studies reporting very little clinically significant effect on tooth whitening.[13–15] Most whitening toothpastes contain abrasives of different sizes and shapes and as the size of the abrasive particles increases, the abrasiveness of a toothpaste also increases leading to increased surface roughness and reduced microhardness of the enamel.

This systematic review and meta-analysis was conceptualized with the hope that this understanding might help in managing toothpaste formulations to bring about tooth whitening without affecting surface roughness and microhardness. The findings would have clinical implications as well as implications for research.

Objective

To assess the effect of whitening toothpastes on the surface roughness and microhardness of human teeth by identifying all relevant literature, evaluating it systematically and synthesizing the data to integrate the findings.

Focus question

We attempted to answer the following question:

Do whitening toothpastes affect the surface roughness and microhardness of human teeth?

Methods

Eligibility criteria

Inclusion criteria

Criteria for including studies in the review were done based on **PICOS**,

i. **P**opulation, or participants and conditions of interest: Extracted human teeth

ii. **I**nterventions or exposures: Brushing with whitening toothpaste

iii. **C**omparisons or control groups: With at least one comparison group

iv. **O**utcomes of interest: Surface roughness and microhardness

v. **S**tudy designs: *In vitro* RCT studies

Exclusion criteria

It was decided to exclude studies in languages other than English and studies where abstracts or full texts were not available.

Information sources
Studies were identified from the electronic databases of Scopus, Embase (EMBASE, RRID:SCR_001650), PubMed (PubMed Central, RRID:SCR_004166), Springer Link, Web of Science (Clarivate Analytics, RRID:SCR_017657) and Cochrane Central Register of Controlled Trials (CENTRAL) (Cochrane Library, RRID:SCR_013000) between February and October 2021.

Search strategy
Search used the following key terms with the Boolean 'OR' operator: "dental enamel" OR "microhardness" OR "surface roughness" OR "*in vitro* study" OR "whitening toothpaste" sort by: relevance, Filters: English.

The selection of articles was completed by two authors (Jamwal N and Rao A) using papers published in the electronic databases, as assessed by the eligibility criteria. Reference checking and hand searching of articles was also done.

Data collection process
Reviewer number 1 (NJ) and reviewer number 2 (AR) screened the articles independently. Any disagreements were resolved by a third author (RS). Covidence® (Veritas Health Innovation, Melbourne, Australia) (RRID:SCR_016485) was used for data screening and data extraction. The CONSORT tool was used for checking relevant content and methodology used in each of the papers reviewed. Systematic review was done followed by meta-analysis, using Review Manager (RevMan version 5.4.1) (RRID:SCR_003581).

Data items
Data was sought for two outcomes namely, surface roughness and microhardness of extracted human teeth, with at least two time points i.e., before and after intervention with a whitening toothpaste. In cases where there were more than one post intervention time points, the final time point was considered. The Covidence data extraction template was customized for this systematic review.

Risk of bias assessment
The quality of the articles was assessed using the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2), which is structured into five domains, risk of bias arising from the randomization process, due to deviations from intended interventions, due to missing outcome data, bias in measurement of the outcome and bias in selection of the reported result.

The Covidence quality assessment template was customized for this study. Reviewer number 1 (NJ) and reviewer number 2 (AR) reviewed the quality of the articles independently. In case of any disagreements, discussions were held to come to a consensus.

Data synthesis
Data was analyzed with the random effects meta-analyses model for continuous data, for the two outcomes of surface roughness and microhardness, using Review Manager (RevMan 5.4.1) (RevMan, RRID:SCR_003581). Forest plots were constructed in Review manager for the two outcomes of surface roughness and microhardness. Publication bias was assessed by constructing funnel plots using Review Manager.

Results
Study selection
A total of 125 articles were obtained on the initial key word search (Table 1), out of which 83 were from Scopus, 25 from Embase, 8 from PubMed/MEDLINE, 4 from Springer Link, 3 from Web of Science and 2 from the Cochrane Library. When the 30 duplicates were removed, we selected 95 articles for level 1 title screening. After title screening, 78 studies were found to be irrelevant, and 17 articles were eligible for full text review. During the full text review, 10 studies were excluded; 5 because the interventions were not in line with the inclusion criteria, 4 because the studies used bovine teeth

Table 1. Characteristics of included studies.

Author, year	Control group	Intervention group/ whitening ingredient	Sample size	Brushing duration	Type of outcome measures	Key conclusions
Bolay 2012	• Control group brushed with water without dentifrice • Colgate Total (control)	• Natural White	8 in each group	Exposed to 20,000 brush strokes	Surface roughness and microhardness	Toothbrushing with whitening dentifrice increased surface roughness values but had no effect on hardness values.
Feitosa 2013	• Colgate Total Advanced Clean (control)	• Colgate Total Advanced Whitening • Colgate Whitening Oxygen Bubbles	12 in each group	Brushed for 20,000 cycles to simulate 10 hours	Surface roughness	Whitening dentifrices increased the surface roughness of enamel.
Rahardjo 2015	• Pepsodent Regular (control)	• Pepsodent Whitening • Formula Sparkling White	20 in each group	Brushed for 840 seconds to simulate 3 months	Surface roughness and microhardness	Tooth brushing with whitening toothpaste for a prolonged time increased enamel roughness and decreased enamel microhardness.
Shamel 2019	• Close Up (control for close up white now) • Sensodyne (control for Sensodyne true white) • Colgate (control for Colgate optic white) • Control with no tooth paste application	• Close up White now • Sensodyne True White • Colgate Optic White	10 in each group	Brushed for 420 minutes, simulating 4 weeks	Surface roughness	Blue covarine containing toothpastes produced less surface abrasion in comparison with blue covarine-free toothpastes.
Alpan Lektemur 2020	• Control group (water brushing only)	• Sensodyne True White • Splat Special Blackwood • Colgate Optic White • Signal White Now • Ipana 3D White • Paradontax Whitening	20 in each group	Brushed for 5 seconds per day for 30 days.	Surface roughness	The two whitening toothpastes i.e., Splat Special Blackwood and Colgate Optic White, reduced enamel roughness, whereas no significant changes were seen with the other whitening toothpastes.
Maden 2021	• Colgate MaxFresh (control)	• İpana White Power	30 in each group	Brushed for 2 min twice a day for 1 week	Surface roughness and microhardness	Ipana White Power toothpaste increased surface roughness and reduced microhardness.
Vural 2021	• Colgate Total (control)	• Body Kingdom • Curaprox Black is White • Colgate Optic White	12 in each group	Hundred and sixty-eight cycles of brushings to simulate 12-weeks.	Surface roughness and microhardness	Except for the Curaprox Black is white, all other toothpastes showed increased surface roughness, while microhardness was not affected in any of the groups.

F1000Research 2022, 11:22 Last updated: 09 MAR 2022

and one because it was an *in vivo* study. Finally, 7 studies were included for systematic review and meta-analysis was conducted on 4 studies (Figure 1).

Characteristics of included studies

The characteristics of included studies are summarized in Table 1. All selected studies were published between 2012 and 2021. The studies used control and comparison groups to evaluate the effects of whitening toothpaste on surface roughness and microhardness of human teeth *in vitro*. Some studies used brushing without toothpaste as the control group[16,17] while others used regular toothpastes as controls.[8,9,18-20] The intervention consisted of a variety of whitening toothpastes like Natural White,[16] Colgate Total Advanced Whitening, Colgate Whitening Oxygen Bubbles,[18] Pepsodent Whitening, Formula Sparkling White,[8] Close up White now, Sensodyne True White, Colgate Optic White,[19] Sensodyne True White, Splat Special Blackwood, Colgate Optic White, Signal White Now, Ipana 3D White, Paradontax Whitening,[17] İpana White Power[9] and Body Kingdom, Curaprox Black is White, Colgate Optic White.[20]

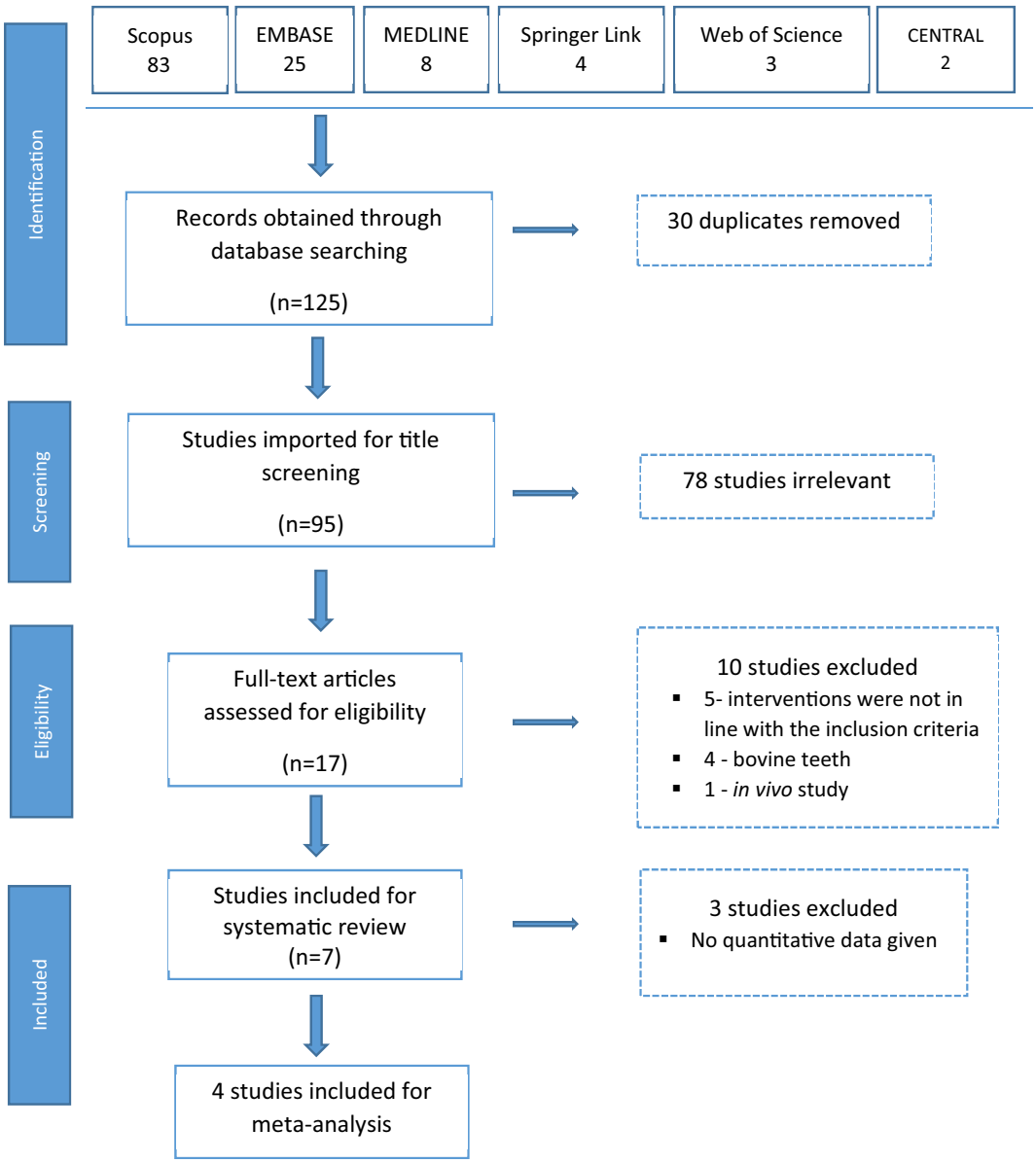

Figure 1. Flow chart of steps in literature search.

The sample sizes varied from 8 per group to 30 per group with four studies having both surface roughness and microhardness as the outcomes and three studies having only one outcome of surface roughness.

Risk of bias in studies

The quality of the 7 articles was assessed using the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2), and is shown in Figure 2. One study showed a high risk of bias and one a low risk of bias. All other 5 studies showed unclear risk of bias. The main concerns were with respect to the risk of bias arising from the randomization process, risk of bias due to deviations from intended interventions and risk of bias in measurement of the outcome.

The study[19] with high risk of bias not only gave no information on the random sequence allocation, but also reported the presence of unsolved baseline differences between intervention groups suggesting a problem with the randomization process. All studies with unclear risk of bias showed lack of information with respect to the random allocation sequence, blinding of people delivering the intervention and blinding of the outcome assessors.

Meta-analysis

We used random-effects meta-analyses model assuming that underlying effects follow a normal distribution. Among the 7 studies that were included for systematic review, quantitative data was inappropriate for 3 studies[9,17,19] and one[19] showed high risk of bias and therefore these studies could not be included, and meta-analysis was conducted using the remaining 4 studies. Data from the 4 studies[8,16,18,20] selected for meta-analysis were analyzed to create forest plots displaying weights and confidence intervals. Separate forest plots were created for the two outcomes of surface roughness and microhardness.

Forest plot for surface roughness

The I^2 value of 61% indicates moderate heterogeneity. The confidence interval of the combined effect size (diamond) does not include zero and is on the right hand side, indicating that the meta-analytic effect is statistically significant and

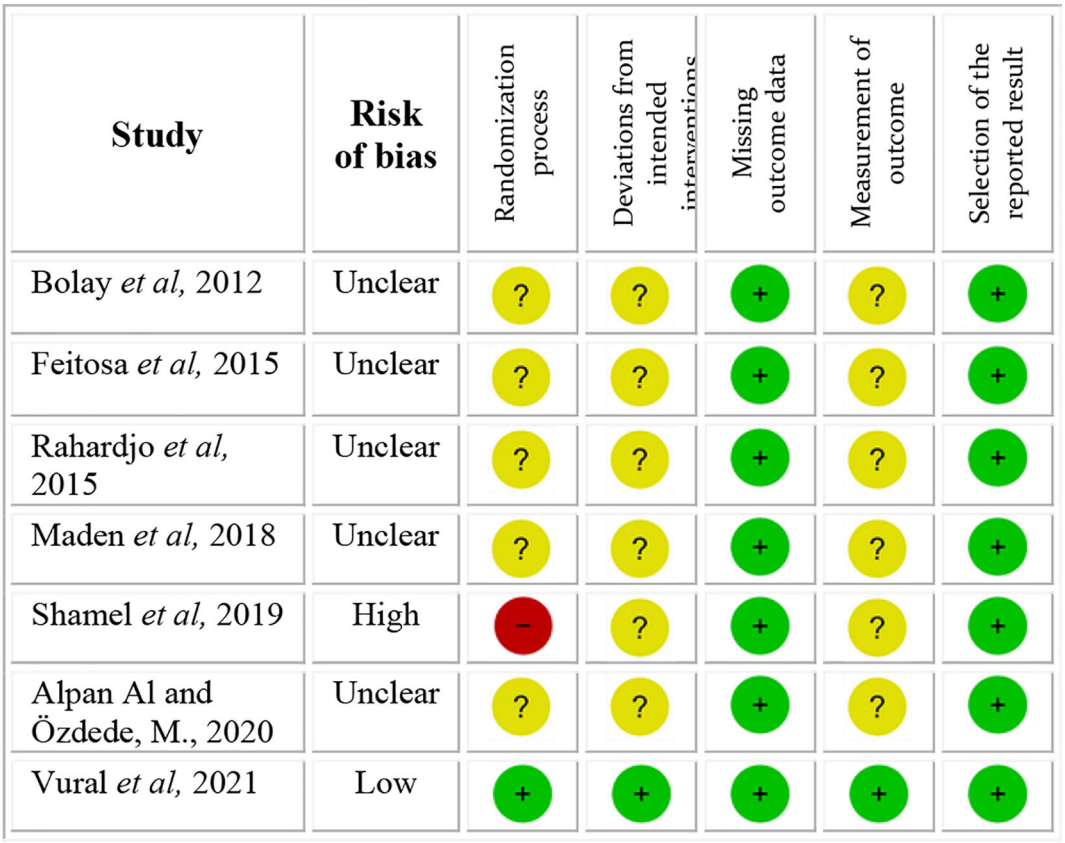

Figure 2. Risk of bias scale.

favoring the control (confidence level of 95%; p-value is less than.05). This shows that the surface roughness value is lesser in the control group when compared with the intervention group. The corresponding Z value is 2.06 and the p value is 0.04 (Figure 3).

Forest plot for microhardness

Since I^2 value is 98% showing high heterogeneity, the results need to be interpreted with caution. The confidence interval of the combined effect size (diamond) does not include zero and is on the left hand side, indicating that the meta-analytic effect is statistically significant and favoring the experimental group (confidence level of 95%; p-value is less than 0.05). This shows that the microhardness value is lesser in the intervention group when compared with the control group. The corresponding Z value is 2.10 and the p value is 0.04 (Figure 4).

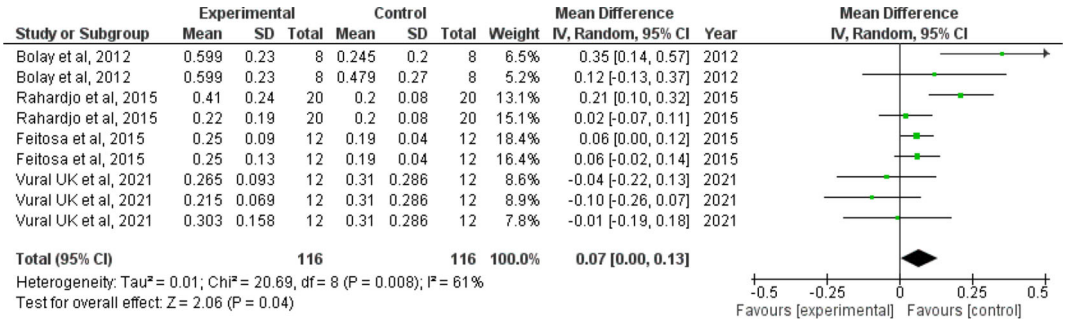

Figure 3. Forest plot comparing the surface roughness of enamel of controls with those brushed with whitening toothpaste.

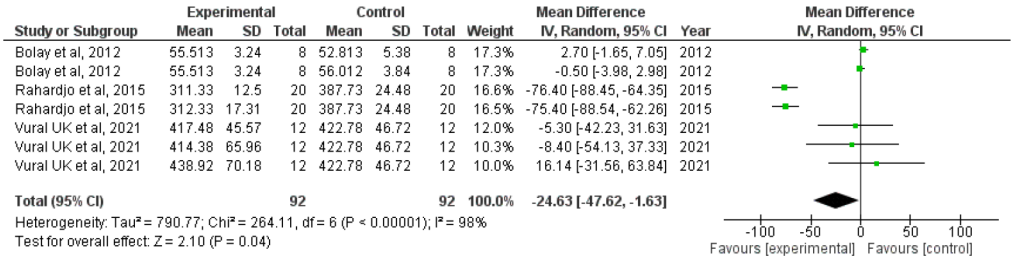

Figure 4. Forest plot comparing the microhardness of enamel of controls with those brushed with whitening toothpaste.

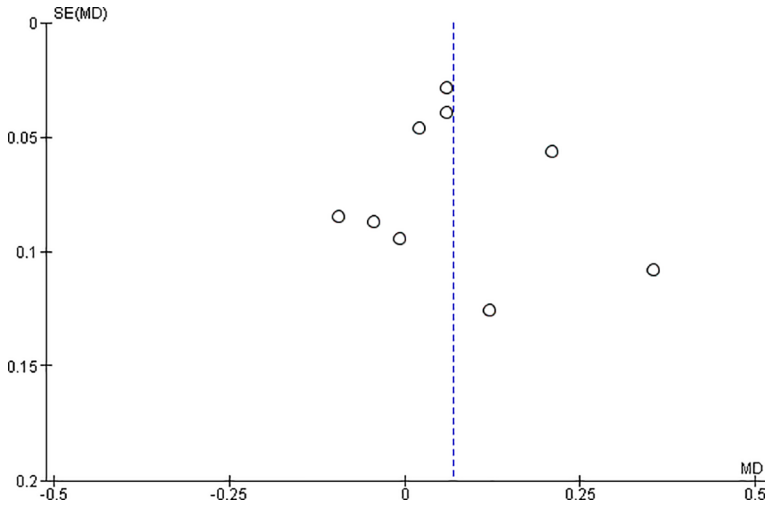

Figure 5. Funnel plot for surface roughness.

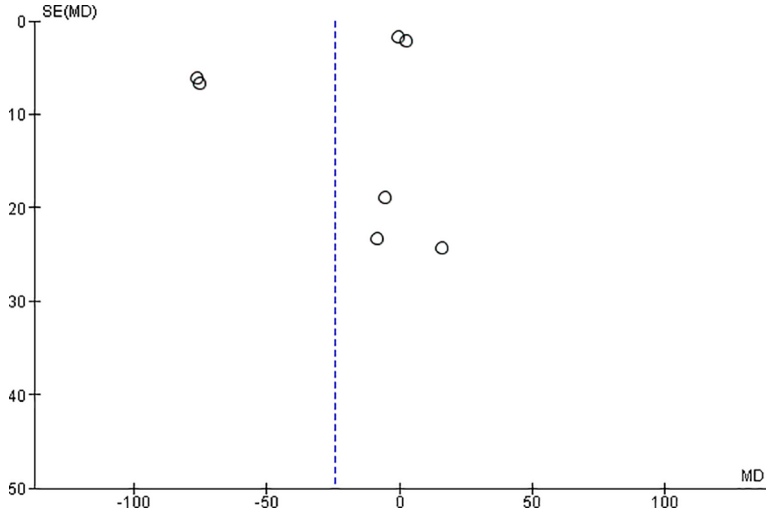

Figure 6. Funnel plot for microhardness.

Funnel plot:

The observed effect sizes were more or less symmetrically distributed around the combined effect size, in both the outcomes, indicating no asymmetry in the distribution of effect sizes and hence no evidence of publication bias (Figures 5 & 6).

Discussion

Whitening toothpastes are easily available over the counter without a prescription. The ingredients of a whitening paste range from abrasives such as hydrated silica, calcium carbonate to whitening agents like perlite, peroxides, activated charcoal, blue covarine, hydrogen peroxide and microbeads.[1] Ideally, whitening toothpastes must remove stains and improve tooth color. However, studies[8,9,16,18,20] have shown that whitening toothpastes also have deleterious effect on the mineral content of enamel resulting in increased surface roughness and reduced microhardness. This systematic review was carried out to examine the relationship between whitening toothpastes and surface roughness as well as microhardness of extracted human teeth.

Surface roughness and microhardness are important indications of loss or gain of mineral content in tooth structure which can be used to show the unwanted effect of whitening toothpastes. Among the 7 studies which were included in this systematic review, 5 studies[8,9,16,18,20] reported increase in surface roughness of enamel. However, in the study by Alpan *et al*,[17] among the 6 whitening toothpastes studied, two whitening toothpastes i.e., Splat Special Blackwood and Colgate Optic White, reduced enamel roughness. The study by Shamel *et al*[19] also showed that whitening toothpastes containing blue covarine produced less surface roughness compared to other whitening toothpastes. With respect to the other outcome of microhardness, two studies reported no effect of whitening toothpastes on microhardness[16,20] and two studies reported that whitening toothpastes reduced microhardness.[8,9]

It is crucial to emphasize that the composition of the whitening toothpaste as well as the content and the type of whitening agent might affect the surface roughness and microhardness of the enamel surface. Moreover, the simulation of toothbrushing and the duration and frequency of its application were different in the 7 studies included for the systematic review, which could have influenced the outcomes.

When we analyzed the forest plot for surface roughness, we found that the meta-analytic effect is statistically significant with surface roughness value being higher in the intervention group i.e., the group which was administered the whitening toothpaste. When the forest plot for microhardness was analyzed, we found that the meta-analytic effect was statistically significant with the microhardness value being lesser in the intervention group.

Since the I^2 value was found to be 61% and 98% in the forest plot for surface roughness and microhardness indicating moderate and high heterogeneity respectively, the pooled statistics need to be interpreted with caution. However, it is also prudent to note that I^2 value is not a measure of absolute heterogeneity. Rather, it tells us what proportion of the observed variance reflects variance in true effect sizes rather than sampling error.[21]

Since this meta-analysis is based on *in vitro* studies and we have also partitioned the data for analysis, the I^2 value may reflect the extent to which confidence intervals from the included studies overlap with each other.

Limitations of the included evidence

All studies except one gave no information about the random allocation sequence, blinding of people delivering the intervention and blinding of the outcome assessors. Although these are *in vitro* studies, randomization plays a crucial role in minimizing bias. The studies included in this systematic review have used toothpastes containing different types of whitening agents such as hydrogen peroxide, charcoal and blue covarine. A few studies[17,19] have shown that some whitening agents produced less surface roughness when compared to other whitening agents. It is important that studies incorporate the exact whitening method used so that it can be correlated with the changes in surface roughness and microhardness.

Conclusions

Implications for practice: Although whitening toothpastes typically can lighten tooth color by about one or two shades, there is some evidence to show that these toothpastes also affect the mineral content of teeth by increasing surface roughness and reducing microhardness. Therefore, dental professionals need to educate their patients to be cautious regarding the prolonged use of home use whitening toothpaste.[22]

Implications for policy: More evidence and further research are needed to identify the type of whitening agent which will whiten the tooth effectively while maintaining the integrity of the tooth structure.

Implications for future research: This systematic review and meta-analysis has provided some evidence that whitening toothpastes do affect the surface roughness and microhardness of human teeth. However, further research with robust methodology, reducing the risk of bias, needs to be conducted to definitively establish the role of abrasive and whitening components in increasing the surface roughness and microhardness of human enamel.

Registration and protocol

Since this was a systematic review and meta-analysis of *in vitro* studies, it could not be registered in PROSPERO. However, the review protocol can be found in the *Extended data*.[23]

Data availability

Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

Extended data

Figshare: Effect of whitening toothpaste on surface roughness and micro hardness of human teeth - A systematic review and meta-analysis, https://doi.org/10.6084/m9.figshare.17128811[23]

The project contains the following extended data:

- Protocol.docx

Reporting guidelines

Figshare: Effect of whitening toothpaste on surface roughness and micro hardness of human teeth - A systematic review and meta-analysis. https://doi.org/10.6084/m9.figshare.17128811[23]

The project contains the following reporting guidelines:

- PRISMA checklist.docx
- PRISMA flow chart.docx

References

1. Vaz VT, Jubilato DP, Oliveira MR, *et al.*: **Whitening toothpaste containing activated charcoal, blue covarine, hydrogen peroxide or microbeads: which one is the most effective?.** *J. Appl. Oral Sci.* 2019; **27**: e20180051.
PubMed Abstract | Publisher Full Text

2. Dietschi D, Benbachir N, Krejci I: **In vitro colorimetric evaluation of the efficacy of home bleaching and over-the-counter bleaching products.** *Quintessence Int.* 2010; **41**(6): 505–516.
PubMed Abstract

3. Watanabe MM, Rodrigues JA, Marchi GM, *et al.*: ***In vitro* cariostatic effect of whitening toothpastes in human dental enamel microhardness evaluation.** *Quintessence Int.* 2005 Jun; **36**(6): 467–473.
PubMed Abstract

4. Sharif N, MacDonald E, Hughes J, *et al.*: **The chemical stain removal properties of 'whitening' toothpaste products: studies *in vitro.*** *Br. Dent. J.* 2000; **188**: 620–624.
PubMed Abstract | Publisher Full Text

5. Epple M, Meyer F, Enax J: **A critical review of modern concepts for teeth whitening.** *Dent. J.* 2019; **7**(3): 79.
PubMed Abstract | Publisher Full Text

6. Joiner A: **Whitening toothpastes: a review of the literature.** *J. Dent.* 2010; **38 Suppl 2**(38): e17–e24.
PubMed Abstract | Publisher Full Text

7. Viscio D, Gaffar A, Fakhry-Smith S, *et al.*: **Present and future technologies of tooth whitening. Compendium of continuing education in dentistry. (Jamesburg, NJ: 1995).** *Supplement.* Jan 2000; (28): S36–S43. quiz S49.
PubMed Abstract

8. Rahardjo A, Gracia E, Riska G, *et al.*: **Potential side effects of whitening toothpaste on enamel roughness and microhardness.** *Int. J. Clin. Prev. Dent.* 2015 Dec 30; **11**: 239–242.
Publisher Full Text

9. Maden EA, Altun C, Polat GG, *et al.*: **The *In vitro* Evaluation of the effect of xyliwhite, probiotic, and the conventional toothpastes on the enamel roughness and microhardness.** *Niger. J. Clin. Pract.* 2018; **21**(3): 306–311.
PubMed Abstract | Publisher Full Text

10. Fearon J: **Tooth whitening: concepts and controversies.** *J. Ir. Dent. Assoc.* 2007 Sep 1; **53**(3): 132–140.
PubMed Abstract | Publisher Full Text

11. Markowitz K: **Pretty painful: why does tooth bleaching hurt?.** *Med. Hypotheses.* 2010 May 1; **74**(5): 835–840.
PubMed Abstract | Publisher Full Text

12. Kielbassa AM, Maier M, Gieren AK, *et al.*: **Tooth sensitivity during and after vital tooth bleaching: A systematic review on an unsolved problem.** *Quintessence Int.* 2015 Nov 1; **46**(10): 881–897.
PubMed Abstract | Publisher Full Text

13. Walsh TF, Rawlinson A, Wildgoose D, *et al.*: **Clinical evaluation of the stain removing ability of a whitening dentifrice and stain controlling system.** *J. Dent.* 2005 May 1; **33**(5): 413–418.
PubMed Abstract | Publisher Full Text

14. Demarco FF, Meireles SS, Masotti AS: **Over-the-counter whitening agents: a concise review.** *Braz. Oral Res.* 2009 Jun; **23**: 64–70.
PubMed Abstract | Publisher Full Text

15. Silva EM, Maia JN, Mitraud CG, *et al.*: **Can whitening toothpastes maintain the optical stability of enamel over time?.** *J. Appl. Oral Sci.* 2018 Feb; **26**: e20160460.
PubMed Abstract | Publisher Full Text

16. Bolay S, Cakir FY, Gurgan S: **Effects of toothbrushing with fluoride abrasive and whitening dentifrices on both unbleached and bleached human enamel surface in terms of roughness and hardness: an *in vitro* study.** *J Contemp. Dent. Pract. Sep.* 2012; **13**(5): 584–589.
PubMed Abstract | Publisher Full Text

17. Alpan AL, Özdede M: **Investigation of the effects of whitening toothpastes on enamel and cementum surfaces.** *J. Stomatol.* 2020; **73**(2): 55–64.

18. Feitosa DA, Borges BC, Pinheiro FH, *et al.*: **Impact of toothbrushing with a dentifrice containing calcium peroxide on enamel color and roughness.** *Gen. Dent.* 2015; **63**(1): e9–e11.
PubMed Abstract

19. Shamel M, Al-Ankily MM, Bakr MM: **Influence of different types of whitening tooth pastes on the tooth color, enamel surface roughness and enamel morphology of human teeth.** *F1000Res.* 2019 Oct 16; **8**: 1764. eCollection 2019.
PubMed Abstract | Publisher Full Text

20. Vural UK, Bagdatli Z, Yilmaz AE, *et al.*: **Effects of charcoal-based whitening toothpastes on human enamel in terms of color, surface roughness, and microhardness: an *in vitro* study.** *Clin. Oral Investig.* 2021; **25**: 5977–5985.
PubMed Abstract | Publisher Full Text

21. Higgins JPT: **Commentary: Heterogeneity in meta-analysis should be expected and appropriately quantified.** *Int. J. Epidemiol.* 2008; **37**(5): 1158–1160.
PubMed Abstract | Publisher Full Text

22. Carey CM: **Tooth whitening: What we need to know.** *J. Evid. Based Dent. Pract.* 2014 June; **14 Suppl**: 70–76.
PubMed Abstract | Publisher Full Text

23. Jamwal N, Rao A, Shenoy R, *et al.*: **Effect of whitening toothpaste on surface roughness and micro hardness of human teeth - A systematic review and meta analysis. figshare.** *Online Resource.* 2021.
Publisher Full Text

Open Peer Review

Current Peer Review Status: ? ✓ ✓

Version 3

Reviewer Report 09 March 2022

https://doi.org/10.5256/f1000research.121868.r126618

✓ **Harsh priya**
Division of Public Health Dentistry, Centre for Dental Education and Research, All India Institute of Medical Sciences, New Delhi, Delhi, India

All the suggestions addressed.
Thank you.
Best Wishes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Dental Public Health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 2

Reviewer Report 21 February 2022

https://doi.org/10.5256/f1000research.121242.r119761

✓ **Ashish Shrestha**
Department of Public Health Dentistry, College of Dental Surgery, B. P. Koirala Institute of Health Sciences, Dharan, Nepal

The review seems complete with the articles reviewed. Only articles written in English have been reviewed as per the expertise present. The authors have presented a full systematic review and explained the meta-analysis. The study selection as well of the risk of bias has been well explained. The review also contains limitations the authors faced while conducting the review. All in all it is appropriate and fit for indexing.

Are the rationale for, and objectives of, the Systematic Review clearly stated?
Yes

Are sufficient details of the methods and analysis provided to allow replication by others?
Yes

Is the statistical analysis and its interpretation appropriate?
Yes

Are the conclusions drawn adequately supported by the results presented in the review?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Oral health, dental public health and preventive dentistry

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 22 Feb 2022

Ashwini Rao, Manipal College of Dental Sciences, Mangalore, Manipal Academy of Higher Education, Manipal, India, Mangalore, India

Thank you

Competing Interests: No competing interests were disclosed.

Version 1

Reviewer Report 24 February 2022

https://doi.org/10.5256/f1000research.80145.r119769

?

Harsh priya
Division of Public Health Dentistry, Centre for Dental Education and Research, All India Institute of Medical Sciences, New Delhi, Delhi, India

Dear Authors,

Congratulations on your manuscript.

The systematic review and meta-analysis has defined the rationale and objective behind the conceptualization of this study. They have defined the in vitro randomized control trials that will be included in this review. The methods and analysis are appropriately defined for replication. The statistical analysis and interpretation of data is pertinent. The conclusion of the review that whitening toothpastes typically can lighten tooth colour by about one or two shades is for clinically application for the general public and private practitioners. There is some evidence generated to show that these toothpastes also affect the mineral content of teeth by increasing surface roughness and reducing microhardness. Such reviews can help clinicians and masses to decide on the continuous use of whitening toothpastes.

Few minor comments are as below:

Comment 1: Table 1- Characteristics of included studies
Bolay 2012 - Exposed to 20.000 brush strokes
(It should be 20,000)
Rahardjo 2015 - Brushed for 840 seconds ti simulate 3 months.
(It should probably be 840 minutes. If we calculate to simulate 5 minutes daily for 90 days it comes to 450 minutes, hence 840 seconds seem to be wrongly written)
Alpan Lektemur 2020 - Brushed for 5 seconds per day for 30 days
(5 seconds per day seems a little less. Need to cross check the data. Probably its 5 minutes per day)

Comment 2:
"7 studies that were included for systematic review, quantitative data was inappropriate for 3 studies and one showed high risk of bias and therefore these studies could not be included, and meta-analysis was conducted using the
remaining 4 studies."
Kindly recalculate. If 3 studies were inappropriate and 1 was not included due to high risk of bias. Seven minus four, i.e. three studies should have been included in meta-analysis.

Hopefully this will improve the manuscript.

All the best.

Are the rationale for, and objectives of, the Systematic Review clearly stated?
Yes

Are sufficient details of the methods and analysis provided to allow replication by others?
Yes

Is the statistical analysis and its interpretation appropriate?
Partly

Are the conclusions drawn adequately supported by the results presented in the review?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Dental Public Health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 26 Feb 2022

Ashwini Rao, Manipal College of Dental Sciences, Mangalore, Manipal Academy of Higher Education, Manipal, India, Mangalore, India

Thanks for the suggestions.
The following suggestion was incorporated
Comment 1: Table 1- Characteristics of included studies, Bolay 2012 - Exposed to 20.000 brush strokes (It should be 20,000) - Correction done.
However, for the below comments, no changes were done since the article mentions 5 seconds and not 5 minutes.
Comment 2: Rahardjo 2015 - Brushed for 840 seconds ti simulate 3 months. (It should probably be 840 minutes. If we calculate to simulate 5 minutes daily for 90 days it comes to 450 minutes, hence 840 seconds seem to be wrongly written)
Response: No changes done:
The article mentions brushing time as 5 seconds not minutes. So no changes were done.
Comment 3: Alpan Lektemur 2020 - Brushed for 5 seconds per day for 30 days (5 seconds per day seems a little less. Need to cross check the data. Probably its 5 minutes per day)
Response: No changes done:
The article mentions brushing time as 5 seconds not minutes. So no changes were done
Comment 4: "7 studies that were included for systematic review, quantitative data was inappropriate for 3 studies and one showed high risk of bias and therefore these studies could not be included, and meta-analysis was conducted using the remaining 4 studies." Kindly recalculate. If 3 studies were inappropriate and 1 was not included due to high risk of bias. Seven minus four, i.e. three studies should have been included in meta-analysis.
Response: No changes done:
One study (Shamel et al – Ref 19) had two issues, quantitative data was inappropriate and also showed high risk of bias. So, meta-analysis was conducted using the remaining 4 studies
“Among the 7 studies that were included for systematic review, quantitative data was inappropriate for 3 studies (9 , 17 , 19) and one (19) showed high risk of bias and therefore these studies could not be included, and meta-analysis was conducted using the remaining 4 studies.”

Competing Interests: No competing interests were disclosed.

Reviewer Report 10 February 2022

https://doi.org/10.5256/f1000research.80145.r119759

?

Dimitrios Dionysopoulos
Department of Operative Dentistry, Faculty of Dentistry, School of Health Sciences, Aristotle University of Thessaloniki, Thessaloniki, Greece

The current systematic review and meta-analysis is interesting and well conducted, albeit the data do not add any new information. It is crucial to be emphasize that the composition of the whitening toothpaste, as well as the content and the type of the whitening agent are the factors that mainly affect the surface roughness and microhardness of the enamel surface. Moreover, the simulation of toothbrushing and the duration and frequency of its application can influence those outcomes. It is also important to discuss that the effectiveness of this whitening method is correlated with the changes in surface roughness and microhardness.

Are the rationale for, and objectives of, the Systematic Review clearly stated?
Yes

Are sufficient details of the methods and analysis provided to allow replication by others?
Yes

Is the statistical analysis and its interpretation appropriate?
Yes

Are the conclusions drawn adequately supported by the results presented in the review?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Operative Dentistry

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 11 Feb 2022

Ashwini Rao, Manipal College of Dental Sciences, Mangalore, Manipal Academy of Higher Education, Manipal, India, Mangalore, India

Dear sir,

Thank you for the suggestions. We have incorporated the suggestions given:

1. In the discussion component, we have incorporated the role of the composition of the whitening toothpaste, as well as the content and the type of the whitening agent on the surface roughness and microhardness of the enamel surface, and also the influence of simulation of toothbrushing and the duration and frequency of its application on the outcomes.

2. In the limitation component, we have added a note on the importance of incorporating the exact whitening method used, in the studies, so that it can be correlated with the changes in surface roughness and microhardness.

Competing Interests: No competing interests were disclosed.