Effect of silicon dioxide nanoparticles on the flexural strength of heat-polymerized acrylic denture base material: A systematic review and meta-analysis

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KEYWORDS
PMMA; Denture base; Flexural strength; SiO\textsubscript{2} nanoparticles; Systematic review; Meta-analysis

Abstract  Objective: This study evaluated the influence of silicon dioxide (SiO\textsubscript{2}) nanoparticles on the flexural strength of heat-polymerized denture base materials.

Background: Nanoparticles have been incorporated into the denture base materials in different proportions to enhance the mechanical properties. Recently, the incorporation of SiO\textsubscript{2} nanoparticles at low concentrations has shown promising outcomes.

Materials and Methods: Following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) protocol, this study was designed with the following focused question: “Does the addition of SiO\textsubscript{2} nanoparticles improve the flexural strength of heat-polymerized acrylic resins?” The inclusion criteria included in-vitro studies that assessed the flexural strength of SiO\textsubscript{2} nanoparticle-reinforced heat-polymerized acrylic denture base resins tested according to American Dental Association specifications. The database search involved articles published from 2005 to 2020 on PubMed/MEDLINE, Web of Science, Google Scholar, and Scopus using the following keywords: SiO\textsubscript{2}, nanosilica, silica oxide, nanoparticles, denture base resin, acrylic resin, polymethyl methacrylate, PMMA, flexural strength, and mechanical properties.

Results: Among 167 studies, five papers fulfilled the inclusion criteria and were added for the data analysis and meta-analysis. Proportions of incorporated SiO\textsubscript{2} nanoparticles ranged from 0.25% to 15% and the reported flexural strength values for the reinforced acrylic resin ranged from 41.25 MPa to 124.56 MPa. The meta-analysis revealed no significant effect on the flexural strength...
between the unmodified and the SiO2 nanoparticle-reinforced acrylic resin.  

**Conclusion:** Therefore, no particular concentration of SiO2 nanoparticles could be recommended for heat-polymerized denture base reinforcement.

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### Contents

1. Introduction ................................................................................................................................. 776
2. Materials and methods ............................................................................................................... 776
   2.1. Focused question and study protocol ..................................................................................... 776
   2.2. Eligibility criteria .................................................................................................................. 777
   2.3. Search strategy ..................................................................................................................... 777
   2.4. Study screening, selection, and management ......................................................................... 777
   2.5. Risk of bias evaluation .......................................................................................................... 777
   2.6. Statistical analysis ................................................................................................................ 778
3. Results ......................................................................................................................................... 778
   3.1. Study selection ...................................................................................................................... 778
   3.2. Risk of bias ........................................................................................................................... 778
   3.3. Qualitative data analysis ........................................................................................................ 778
   3.4. Meta-analysis ....................................................................................................................... 780
4. Discussion .................................................................................................................................... 780
5. Conclusions ................................................................................................................................. 781
Appendix A. Supplementary material ............................................................................................. 782
References ........................................................................................................................................ 782

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### 1. Introduction

Heat-polymerized acrylic resin is commonly used to fabricate definitive complete and partial removable dental prostheses (Polychronakis et al., n.d.). It has the features of a natural intra-oral appearance; biocompatibility; simple processing, finishing, and polishing techniques; and cost efficiency (Al-Thobity, 2020; Gad et al., 2019b). However, it has low flexural strength and toughness. A prosthesis fracture may ultimately occur under a functional load and repeated masticatory forces (Gad et al., 2020a; Gad et al., 2019c; Kanie et al., 2000).

Several materials and techniques have been employed to reinforce acrylic resin and improve its flexural properties (Ayaz et al., 2014; Gad et al., 2019a; Ozkir et al., 2018). Recently, the incorporation of nanoparticles into acrylic resin has been investigated (Al-Harbi et al., 2019; Bangera et al., 2020; Gad et al., 2019a) The nanoparticle dimensions range from 1 nm to 100 nm, resulting in a high surface area compared with the volume (Ashton, 2009). The reinforcement effect of nanoparticles for acrylic resin depends on the level of particle dispersion, particle size, and silanization (Du and Zheng, 2007). One of the widely used particles is silica (SiO2) nanoparticles. The addition of SiO2 nanoparticles to dental polymers and other dental composites has been revealed to be effective (Gad et al., 2017; Gad et al., 2020b; Hu et al., 2004; Okada et al., 2014). Gad et al. (2020b) found that adding SiO2 nanoparticles at low concentrations (0.25, 0.5 wt%) to the repaired resin substantially improved the flexural strength.

Numerous in vitro studies have assessed the mechanical properties of the SiO2 nanoparticle-reinforced acrylic resin (Cevik and Yildirim-Bicer, 2018; Jiangkongkho et al., 2018; Karci et al., 2019; Sodagar et al., 2013). The principal mode, which is pertinent to the loading of acrylic denture bases intraorally and in clinical failure, is the flexural strength test. It represents the highest level of stress within the material before the moment of yield (Chitchumnong et al., 1989). Conducting in vitro studies enables the standardization of the specimens’ preparation, allocation, and assessment, necessitating the comparison of the study variables and outcomes.

To the best of the authors’ knowledge and after reviewing the literature, no studies have yet reviewed the influence of SiO2 nanoparticles on the flexural strength of a heat-polymerized acrylic denture base material. Thus, this systematic review aimed to identify and analyze the effect of the incorporation of SiO2 nanoparticles on the flexural strength of heat-polymerized acrylic resin. The null hypothesis is that the incorporation of SiO2 nanoparticles into acrylic resin has no influence on flexural strength.

### 2. Materials and methods

#### 2.1. Focused question and study protocol

The study protocol was carried out following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) model (Faggion, 2012). The focused question of this systematic review was formulated following the PICOS model to lead the literature search as follows: Population (P): denture base resin, heat-polymerized acrylic resin, poly-methylmethacrylate (PMMA); Intervention (I): silica oxide nanoparticles; Comparison (C): the effect of silica oxide nanoparticles in different proportions compared with the con-
The inclusion criteria included in vitro studies that assessed the flexural strength of SiO₂ nanoparticle-reinforced heat-polymerized acrylic denture base resins and compared it with the conventional acrylic resin (control group). Specimens with an adequate size were described clearly in the study methodology, and the specimens’ dimensions were designed and prepared in accordance with the American Dental Association (ADA) specifications/ISO (International Organization for Standardization) 20795. ("ISO 20795–1:2013. Dentistry – base polymer – part 1:denture base polymers. International Organization for Standardization; 2013," n.d.) A three-point bending testing was applied using a standardized universal testing machine to assess the flexural strength property, and the results were statistically analyzed.

Studies out of the dentistry field, studies written in a language other than English, and review papers were excluded from this study. Studies that used acrylic resin other than the heat-polymerized acrylic resin, such as microwave polymerized, autopolymerized, and light polymerized, were omitted from this review. Articles that did not report flexural strength and SiO₂ nanoparticle reinforcement were not eligible for review and analysis. Research that tested flexural strength using techniques other than the three-point bending strength test was also excluded from this study.

2.3. Search strategy

Electronic scientific databases (PubMed/MEDLINE, Web of Science, Google Scholar, and Scopus) were comprehensively searched to find relevant articles published between January 2005 and September 2020. This search was conducted using a combination of the following keywords: SiO₂, nanosilica, silica oxide, nanoparticles, denture base resin, acrylic resin, polymethylmethacrylate, PMMA, flexural strength, and mechanical properties. To ensure that all eligible articles were included, the authors performed a manual search by checking the reference list of relevant review articles.

2.4. Study screening, selection, and management

The authors reviewed the titles to exclude papers that did not fulfill the inclusion criteria. The abstracts were examined for a qualification check whenever the titles were insufficiently illustrative for judgment. After omitting all duplicates, full text publications following the inclusion criteria were retrieved for scrutiny and data extraction. The obtained data from the included studies were tabulated using an electronic format (Microsoft Excel, V14.6.8, Redmond, WA, USA). The data were categorized as follows: authors’ names and year of publication; brand name of nanoparticles; nanoparticles size; silanization; Wt.%; sample size; acrylic resin type/ polymerization cycle; mixing protocol; specimens dimension; testing type/standard; sample conditioning; mean (SD) of flexural strength (MPa); SEM analysis; and outcome (Appendix A Supplementary Material).

2.5. Risk of bias evaluation

The quality of the intended studies was evaluated and rated following the Consolidated Standards of Reporting Trials (CONSORT) guidelines (Faggion, 2012). After evaluating the studies individually, the parameters were presented as yes or no (Table 1). The Cochrane tool for risk of bias was adopted and modified to fulfill the study objective (Table 2). (Faggion, 2012; Higgins et al., 2011) The following criteria were employed to assess the potential risk of bias: calculation of sample size; selection bias, which is relevant to the sample allocation in the intended study, and concealment; blinding status of the operator; matching of the analysis methods with the ADA/ISO standards; and the reported outcomes. A score

| Article Item grade | 1 | 2a | 2b | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|-------------------|---|----|----|---|---|---|---|---|---|---|----|----|----|----|----|
| Alnemel and Mudhaffer 2014 [32] | Yes | Yes | No | No | No | No | No | No | No | Yes | No | Yes | No | No |
| Salman et al 2017 [33] | Yes | Yes | No | No | Yes | No | No | No | No | No | Yes | Yes | No |
| Cevik and Yildirim-Bicer, 2018 [26] | Yes | Yes | Yes | Yes | Yes | No | Yes | No | No | No | Yes | Yes | No |
| Jiangkongkho et al. 2018 [24] | Yes | Yes | Yes | Yes | Yes | No | No | No | No | Yes | Yes | Yes | Yes | No |
| Karei et al 2019 [23] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | Yes | Yes | Yes | No |

(1) Structured summary of trial design, methods, results and conclusions, (2a) scientific background and explanation of rationale, (2b) specific objectives and/or hypothesis, (3) the intervention of each group, including how and when it was administered, with sufficient detail to enable replication, (4) completely defined, pre-specified primary and secondary measured of outcome, including how and when they were assessed, (5) how the sample size was determined, (6) method used to generate the random allocation sequence, (7) mechanism used to implement the random allocation sequence, (8) who generated the random allocation, (9) who was blinded after assignment to intervention, (10) statistical methods used to compare groups, (11) results for each group and estimated size of effect and its precision, (12) trial limitations, addressing sources of potential bias, imprecision, and, if relevant multiplicity of analysis, (13) sources of funding and other support, (14) where to full trial protocol can be accessed.
of zero was given if the study clearly described the previous criteria. If the data were insufficient or ambiguous, the score given was 1. Once the study undisclosed a particular setting, the score given was 2. Studies obtaining an overall score of 0–3 had a low risk of bias, 4–7 had a moderate risk, and 8–10 had a high risk. The authors performed the assessment separately and discussed it independently to sort out any ambiguity.

2.6. Statistical analysis

The meta-analysis was conducted based on the study objective to analyze the flexural strength property of the included studies. A random effect model was applied using Review Manager (RevMan version 5.4; The Cochrane Collaboration, 2020). The SiO₂ nanoparticle groups subjected to the meta-analysis were 1%, 3%, 5%, and 7%, and the other groups (0.25%, 0.50%, 10%, and 15%) were not included because of inadequate outcomes for comparison. A 95% confidence interval (Z) was used to create the forest plot. The inconsistency I² test was applied to calculate the heterogeneity between the study results. When the I² value was greater than 50%, heterogeneity was counted substantial. The funnel plot could not be applied because of the limited number of studies included in the meta-analysis for each nanoparticle proportion (n < 10).

3. Results

3.1. Study selection

The primarily search throughout the four scientific databases yielded 167 scientific publications (Fig. 1). Among them, 23 were duplicates, 81 had irrelevant titles, and 5 were not published in English and thus were excluded. A total of 58 scientific papers were extensively scrutinized for abstract review, and 14 were found to be related to this review question. After scrutinizing these articles, five fulfilled the inclusion criteria and were added in the data analysis, while the remaining nine were excluded because they incorporated with microsilica, employed acrylic resin other than heat-polymerized, or did not follow the ADA/ISO standards. The methodology, results, and outcomes of these studies are summarized in (Appendix A Supplementary Material).

3.2. Risk of bias

The risk of bias of the intended studies is shown in Table 2. Among the five studies (Alnamel and Mudhaffer, 2014; Cevik and Yildirim-Bicer, 2018; Jiangkongkho et al., 2018; Karci et al., 2019; Salman et al., 2017), one (Alnamel and Mudhaffer, 2014) had a high risk, three (Cevik and Yildirim-Bicer, 2018; Jiangkongkho et al., 2018; Salman et al., 2017) had a moderate risk, and one (Karci et al., 2019) had a low risk of bias. The high risk rating was mainly due to the failure to report the sample size calculation, assessment methods, and blinding of investigators. The moderate risk assessment referred to the failure to blind the investigators and to state the method of sample size calculation.

3.3. Qualitative data analysis

All studies included in this review were in vitro laboratory based and used SiO₂ nanoparticles in different proportions to reinforce heat-polymerized acrylic denture base resins. The applied sample size was set to 10 specimens for three studies (Alnamel and Mudhaffer, 2014; Karci et al., 2019; Salman et al., 2017) and eight specimens for two studies (Cevik and Yildirim-Bicer, 2018; Jiangkongkho et al., 2018) for the control and the test groups.

The incorporated weight proportions of SiO₂ nanoparticles varied among the studies and ranged from 0.25% to 15% (Jiangkongkho et al., 2018). The incorporated SiO₂ nanoparticles were prepared in different sizes, with the smallest at 15 nm (Karci et al., 2019) and the largest at < 100 nm (Alnamel and Mudhaffer, 2014). Salman et al. (Salman et al., 2017) investigated two types of SiO₂ nanoparticles: 70-nm crystalline nanosilica sand (NSS) and 50-nm amorphous nanosilica (NS). Three studies (Alnamel and Mudhaffer, 2014; Karci et al., 2019; Salman et al., 2017) did not state whether the nanoparticles were silanized, and two studies (Cevik and Yildirim-Bicer, 2018; Jiangkongkho et al., 2018) performed the silanization procedure of the SiO₂ nanoparticles before their incorporation into the resin. Four studies added the SiO₂ nanoparticles into the methylmethacrylate monomer (Alnamel and Mudhaffer, 2014; Cevik and Yildirim-Bicer, 2018; Jiangkongkho et al., 2018) and one study added it to the PMMA powder before mixing (Karci et al., 2019).

All studies performed the water bath method for heat polymerization. Three studies (Alnamel and Mudhaffer, 2014; Cevik and Yildirim-Bicer, 2018; Jiangkongkho et al., 2018) conducted the short cycle, one study (Karci et al., 2019) implemented the long cycle, and one study (Salman et al., 2017) did not describe the heat polymerization technique in detail. Three studies (Alnamel and Mudhaffer, 2014; Jiangkongkho et al., 2018; Salman et al., 2017) conditioned the specimens through water immersion before testing, and two studies did not report
The results of the studies were diverse regarding the mean value of the flexural strength for both the unmodified and reinforced groups. The lowest value in the control groups was 34.5 MPa (Salman et al., 2017), whereas the highest value was 188.3 MPa (Cevik and Yildirim-Bicer, 2018). Conversely, the highest flexural strength mean value in the reinforced groups was 124.56 MPa (Alnamel and Mudhaffer, 2014) after a 5% SiO₂ nanoparticle reinforcement, whereas the lowest value was 41.25 MPa after the incorporation of 3% SiO₂ nanoparticles (Salman et al., 2017). Cevik and Yildirim-Bicer (2018) and Salman et al. (2017) (NS) showed a direct relation in which the flexural strength increased once the percentage of the nanoparticles increased, whereas the results of Karci et al. (2019) exhibited a decrease in the flexural strength upon an increase in the nanoparticle percentage. The other studies (Alnamel and Mudhaffer, 2014; Jiangkongkho et al., 2018; Salman et al., 2017) showed a limited increase in flexural strength through the addition of low concentrations of nanoparticles and a decrease in flexural strength when the nanoparticle addition reached the highest tested concentrations.

Four studies (Cevik and Yildirim-Bicer, 2018; Jiangkongkho et al., 2018; Karci et al., 2019; Salman et al., 2017) performed SEM analysis to assess the surface characteristics of the control and reinforced specimens. Cevik and Yildirim-Bicer (2018) reported that the addition of 5% nanoparticles did not accompany an eminent cluster of the nanoparticles referred to in the SCA application. Jiangkongkho et al. (2018) found that at high magnification, the nanoparticles acted as a hindrance to prevent or deviate crack propagation. Karci et al. (2019) found that the nanoparticles at a high concentration became agglomerated, and this could explain the lower flexural strength at a high concentra-
tion (5%). Salman et al. (Salman et al., 2017) reported a homogenous distribution of nanoparticles that filled the pores in a polymer matrix, formulating a dense structure of PMMA/NS nanocomposites.

### 3.4. Meta-analysis

Four meta-analyses, including the five studies, were carried out by generating forest plots. Salman et al. (2017) analyzed the two types of nanosilica (NS and NSS) separately. The flexural strength mean values and SD were employed based on the respective SiO$_2$ nanoparticle proportions.

Fig. 2 shows the forest plot for the addition of 1% SiO$_2$ nanoparticles in three studies (Cevik and Yildirim-Bicer, 2018; Jiangkongkho et al., 2018; Karci et al., 2019). The addition of 1% SiO$_2$ nanoparticles had no significant effect on the flexural strength compared with the control group. The mean difference (MD) of this analysis was $-19.52$, the 95% confidence interval (CI) was $-59.31$–$20.30$, and the total number of specimens was 46. All included studies showed a high level of heterogeneity ($I^2$ inconsistency test was 99%).

The forest plot in Fig. 3 presents the effect of adding 3% SiO$_2$ nanoparticles in three studies (Alnamel and Mudhaffer, 2014; Karci et al., 2019; Salman et al., 2017), with one study having two types of nanosilica. This nanoparticle proportion did not significantly improve the flexural strength compared with the control group. The MD was $4.82$, the 95% CI was $-5.92$–$15.56$, and the total number of specimens was 74. A substantial level of heterogeneity was observed in this analysis ($I^2$ inconsistency test was 93%).

The meta-analysis of the addition of 5% SiO$_2$ nanoparticles is presented in Fig. 4. The forest plot showed no remarkable increase in flexural strength with the addition of 5% nanoparticles in the unmodified control group. A substantial level of heterogeneity of the included studies was observed ($I^2$ inconsistency test was 98%). The number of studies (Alnamel and Mudhaffer, 2014; Cevik and Yildirim-Bicer, 2018; Jiangkongkho et al., 2018; Karci et al., 2019; Salman et al., 2017) was 5 (with one of them investigating two types of nanosilica), the MD was $-7.02$, the 95% CI was $-20.64$–$6.59$, and the total number of specimens was 106.

### 4. Discussion

This systematic review was conducted to investigate the influence of SiO$_2$ nanoparticles on the flexural strength of a heat-polymerized acrylic denture base resin. According to the meta-analysis conducted to analyze the effect of the weight proportions (1%, 3%, 5%, and 7%) of four nanoparticles, no significant enhancement was observed in the flexural strength value of the unmodified acrylic resin (control group), although two of these proportions (3% and 7%) had a positive effect based on the effect estimate by increasing the flexural strength values by 4.82 MPa and 9.60 MPa, respectively. Thus, the null hypothesis of this study was accepted. The meta-analysis showed substantial heterogeneity among the included studies based on the $I^2$ inconsistency test ranging from 93% to 99%. This high heterogeneity could be due to variations in the sample size, testing method, size of SiO$_2$ nanoparticles, concentration of SiO$_2$ nanoparticles, silanization process, resin type, resin composition, polymerization cycle of the resin, and the conditioning of the specimens.

The incorporation of SiO$_2$ nanoparticles to the acrylic resin has been suggested to promote the mechanical properties. (Balos et al., 2014; Hu et al., 2004; Lazzara and Milioto, 2010) Balos et al. (Balos et al., 2014) reported that microhardness and fracture toughness were improved at low concentrations. However, increasing the content of SiO$_2$ nanoparticles resulted in the reduction of mechanical properties. Some stud-
ies included in this review showed similar effects of flexural strength increasing at low concentrations of SiO₂ nanoparticles and decreasing at high levels (Alnamel and Mudhaffer, 2014; Jiangkongkho et al., 2018; Salman et al., 2017). This behavior could be attributed to the fact that the addition of nanoparticles at low concentrations could lead to the distribution of nanoparticles homogenously within the polymer matrix spaces and the creation of an interfacial bond between the nanoparticles and the polymer matrix, which could arrest or deviate the crack and improve flexural strength (Cevik and Yildirim-Bicer, 2018; Hafizah et al., 2013; Karci et al., 2019; Sivaraman et al., 2006).

One of the methods that have been investigated to reduce surface energy and inhibit nanoparticle clustering is the silanization of nanoparticles (Chandra et al., 2008). This method is applied by using an SCA as a dispersing agent, such as γ-methacrylo-propyl-trimethoxysilane, to treat the SiO₂ nanoparticles (Kanie et al., 2004). Owing to the functional groups in its chemical structure, the coupling agent can form a strong bond between the SiO₂ nanoparticles and the polymer matrix and positively enhance the mechanical properties (Katsikis et al., 2007).

Based on the current ISO protocol, specimens should be immersed in water for 50 ± 2 h at 37 °C prior to flexural strength testing. (ISO 20795–1:2013. Dentistry – base polymer – part 1: denture base polymers International Organization for Standardization; 2013, n.d.). Two studies (Alnamel and Mudhaffer, 2014; Jiangkongkho et al., 2018) followed the ISO standards, two studies (Cevik and Yildirim-Bicer, 2018; Karci et al., 2019; Sivaraman et al., 2006) failed to state the specimens’ conditioning procedure, and one study exceeded the ISO standards (Salman et al., 2017). Salman et al. (2017) left the unreinforced and reinforced specimens in water for 14 days at room temperature prior to testing. The flexural strength value for the control group was 34.5 MPa and that for the reinforced group was 41.25–60 MPa. This reduction in flexural strength can be attributed to the long immersion of the specimens in water, the molecules of which diffuse into the polymer matrix and fill the voids created from leaching out of the water-soluble particles in acrylic resin (Arima et al., 1995; Gad et al., 2020a; Vallittu et al., 1995).

In the studies involved in this review, a considerable variation was found in the polymerization cycle used for the specimens. Moreover Karci et al. (2019), polymerized the specimens using a long curing cycle by keeping the specimens in a water bath at 74 ± 1 °C for 8 h and then boiling for 2 h, whereas other studies used a short curing cycle at different extents. This diversity in curing cycles could have affected the flexural strength of acrylic resin. Seo et al. (2007) found that the polymerization of acrylic resin at 73 °C for 90 min and then at 100 °C as a boiling temperature for 30 min (short cycle) substantially increased the flexural strength compared with the polymerization at 71 °C for 9 h. This effect can be justified by the degree of residual monomer conversion in which the residual monomer content is most likely higher in the long cycle than in the short cycle, consequently affecting the flexural strength of acrylic resin (Azzarri et al., 2003; Gungor et al., 2017; Urban et al., 2007).

This review has some limitations, such as the limited number of studies assessing the effect of SiO₂ nanoparticle addition on the flexural strength of heat-polymerized acrylic resin. As the analysis of the review was limited to heat-polymerized acrylic resin, the results cannot be adapted to other types of acrylic resins, such as autopolymerized, light polymerized, and microwave and autoclave polymerization. Moreover, the mechanical properties other than flexural strength were not analyzed.

5. Conclusions

The values of the flexural strength property of SiO₂ nanoparticle-reinforced heat-polymerized acrylic resin were diverse among the analyzed studies depending on the concentration, dimension, geometry, and silanization of nanoparticles. The other factors affecting the results were the specimens’ preparation, conditioning of the specimens, polymerization cycle, and testing protocol. The meta-analysis revealed no significant effect on flexural strength between the unmodified and the SiO₂ nanoparticle-reinforced acrylic resin. Thus, no particular concentration of SiO₂ nanoparticles could be recommended for acrylic resin reinforcement.
Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sdentj.2021.08.008.

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Effect of silica oxide nanoparticles on the flexural strength of heat-polymerized acrylic denture base material

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