

REVIEW ARTICLE

EVALUATION OF FLEXURAL STRENGTH OF DENTURE-BASED MATERIALS REINFORCED WITH AL₂O₃, SiO₂, TiO₂, AND ZrO₂ NANOPARTICLES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Background: With the introduction of nanotechnology in dentistry, the use of nanoparticles to strengthen acrylic resins has received much attention. The aim of the present study was to evaluate the effects of different percentages (1%, 2%, 3% & 5%) of Al₂O₃, SiO₂, TiO₂, and ZrO₂ nanoparticles in acrylic resin on the bending strength.

Materials & Methods: The PRISMA 2020 Checklist was used to carry out a systematic review and meta-analysis as the basis for the current investigation. Up until 23 October 2022, systematic literature searches were conducted on Scopus, PubMed, EBSCO, Web of Science, ISI Web of Knowledge, and Embase. Then, a fixed-effect model and the inverse-variance method were been utilized to generate the 95% confidence interval for mean differences. Data from the meta-analysis has been analyzed utilizing Stata/MP v.17 software.

Results: A review of abstracts from 800 studies was conducted in the initial review of the study to eliminate duplicates; full texts of 391 studies were reviewed by two authors, and 14 studies were ultimately chosen. The mean flexural strength difference between the control group and the 1% Al₂O₃ reinforcement was -6.19 (MD, -6.19 95% CI -8.26, -4.11; p=0.00). The mean flexural strength difference between the control group and the 3% SiO₂ reinforcement was 4.58 (MD, 4.58 95% CI 3.61, 5.56; p=0.00). The mean flexural strength difference between the control group and the 1% TiO₂ reinforcement was -4.08 (MD, -4.08 95% CI -35.03, 26.87; p=0.80).

Conclusions: It can be concluded from the present meta-analysis that the properties of polymers reinforced with nanoparticles depend on their type and concentration.

KEY WORDS: Flexural strength; Nanoparticles; Resin-Bonded; Aluminum oxide; Titanium dioxide; Zirconium oxide.

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INTRODUCTION

Prosthetic rehabilitation of edentulous patients is typically conducted using poly(methyl methacrylate)

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(PMMA). This method has many fans due to its low cost and high patient satisfaction, and aesthetic results.¹ However, this method has disadvantages, such as low failure resistance and poor mechanical properties.² Among the most common problems are midline fractures of complete upper jaw prostheses. Studies have shown that more than half of the patients who had complete dentures prosthetics, fractured their dentures after three years.³ Generally, heat-polymerized acrylic resins are used for the base of artificial teeth.⁴ Also, one of the common methods is to use microwave energy for PMMA polymerization, which is done in less time than thermal polymerization.⁵ According to the ISO

1567 standard, dental base polymers must have a minimum flexural strength value of 65 MPa,⁶ which should not be added less than this amount for the strength of any filler material. Various methods have been used to increase flexural strength, including metal oxides, metal wires, and fibers; However, with the introduction of nanotechnology in dentistry, the use of nanoparticles to strengthen acrylic resins has received much attention.^{7,8} Studies have shown that incorporating inorganic nanoparticles in PMMA can improve mechanical properties.⁹⁻¹¹ The properties of polymer nanocomposites depend on several factors such as size and shape, as well as their concentration, and the type of composition of nanoparticles are also very important.¹² Among the most common nanoparticles used in dentistry are silver nanoparticles, aluminum oxide nanoparticles, silicon dioxide nanoparticles, zirconium dioxide nanoparticles (ZrO₂), and titanium dioxide nanoparticles (TiO₂).¹³ Due to the importance of examining the flexural strength in the resistance of the prosthesis base, the objective of the current research is to investigate the flexural strength of different types of nanoparticles and provide strong evidence in this field. Therefore, the question of the present study was whether the different percentages of Al₂O₃, SiO₂, TiO₂, and ZrO₂ nanoparticles in acrylic resin affect the bending strength.

MATERIALS AND METHODS

Search strategy

This study involved the systematic review and meta-analysis of pertinent articles using the PRISMA 2020 Checklist as a guide.¹⁴ Until 23 October 2022, keywords associated with the study's goals were searched in PubMed, Scopus, Science Direct, ISI, Web of Knowledge, and Embase. Using the Google Scholar search engine, related articles were also identified.

The selection process, Data items, Data collection

The following items were included in a checklist: name of the author, year of publication, sample size, test Standard, specimen size, storage, details, and fraction weight in percentage for each Al₂O₃, SiO₂, TiO₂, ZrO₂ Nanoparticles were extracted and reported in Table 3, 4, 5 and 6. In addition, data from the studies were extracted for the meta-analysis, including flexural strength. Each article was selected based on the inclusion criteria, each record was independently screened by two reviewers, and each report was retrieved.

Eligibility criteria

Inclusion criteria: in vitro laboratory-based studies, studies evaluating the flexural strength of various nanoparticle-reinforced materials, studies with a control group (conventional acrylic resin), studies that reported Test Standards, Specimens with adequate

size, and Studies published in English.

Exclusion criteria: Review papers, Case reports, case studies.

Risk of bias assessment of the study

Assessment of the research' quality was based on a modified version of CONSORT Criteria (Pre-clinical reporting guidelines for dental materials,¹⁵ there have been 14 items in each study, and each parameter was rated as yes or no. These items have been:

An organized explanation of the trial's design, methods, findings, and conclusions that includes the scientific justification and background as well as the goals, hypotheses, and interventions of each group, as well as how and when they were applied, in enough detail to allow replication and in a manner that is clearly defined. It is necessary to identify the method by which the random allocation sequence is produced, the mechanism by which the random allocation sequence is implemented, and the person in charge of producing the random allocation sequence, who was blinded after the intervention was applied, as well as the method of determining sample size and generating random allocation sequences as well as the method by which primary and secondary outcomes are measured. A full description of the trial protocol, the statistical methods utilized for comparing the groups, the outcomes for every group, the amount and precision of the impact, and the limitations of the trial, how bias and imprecision can be addressed, and if necessary, access can be made to the variety of analyses, funding sources, and other sources of assistance.

Based on the Cochrane risk of bias tool, a risk of bias tool was developed and modified for use in this study. In this tool, A score of 2, 1, or 0 was assigned to each item; A sum of scores 0 to 3 is related to a low risk of bias, and a sum of scores 4 to 7 is connected with a moderate risk of bias, and a sum of scores 8 to 10 is associated with a high risk of bias. A score of 0 was the lowest and a score of 10 was the highest in this tool.¹⁶

Data analysis

Analysis of data was conducted with STATA/MP. V17 software. Then, utilizing a fixed-effect model and the inverse-variance method for mean differences, the 95% confidence interval was calculated. Potential heterogeneity was addressed using random effects and I² indicators. I² values above 50% suggest moderate to high heterogeneity, whereas I² values below 50% indicate low heterogeneity.

RESULTS

Study selection

Eight hundred forty-five (845) articles relating to the keywords were identified in the initial search. Two hundred and thirty seven (237) of these dealt with

Al₂O₃, 241 with SiO₂, 281 with TiO₂, and 86 with ZrO₂. There were 28 duplicate studies, 12 records that were marked ineligible by automated tools, and five articles that were removed due to other factors. In the next step, After reviewing abstracts of 800 articles, 391 articles were excluded from the research based on the exclusion criteria. After reviewing 391 articles, 377 were excluded according to inclusion criteria, and 14 were selected (Figure 1).

The risk of bias in research

The risk of bias assessment tool determined that two articles had a high risk of bias, five articles had a low risk of bias, and seven articles had a moderate risk of bias (Tables 1 and 2).

Study characteristics

An overview of the information gleaned from the research is presented in tables 3, 4, 5, and 6. Each table is related to the characteristics of Nanoparticles.

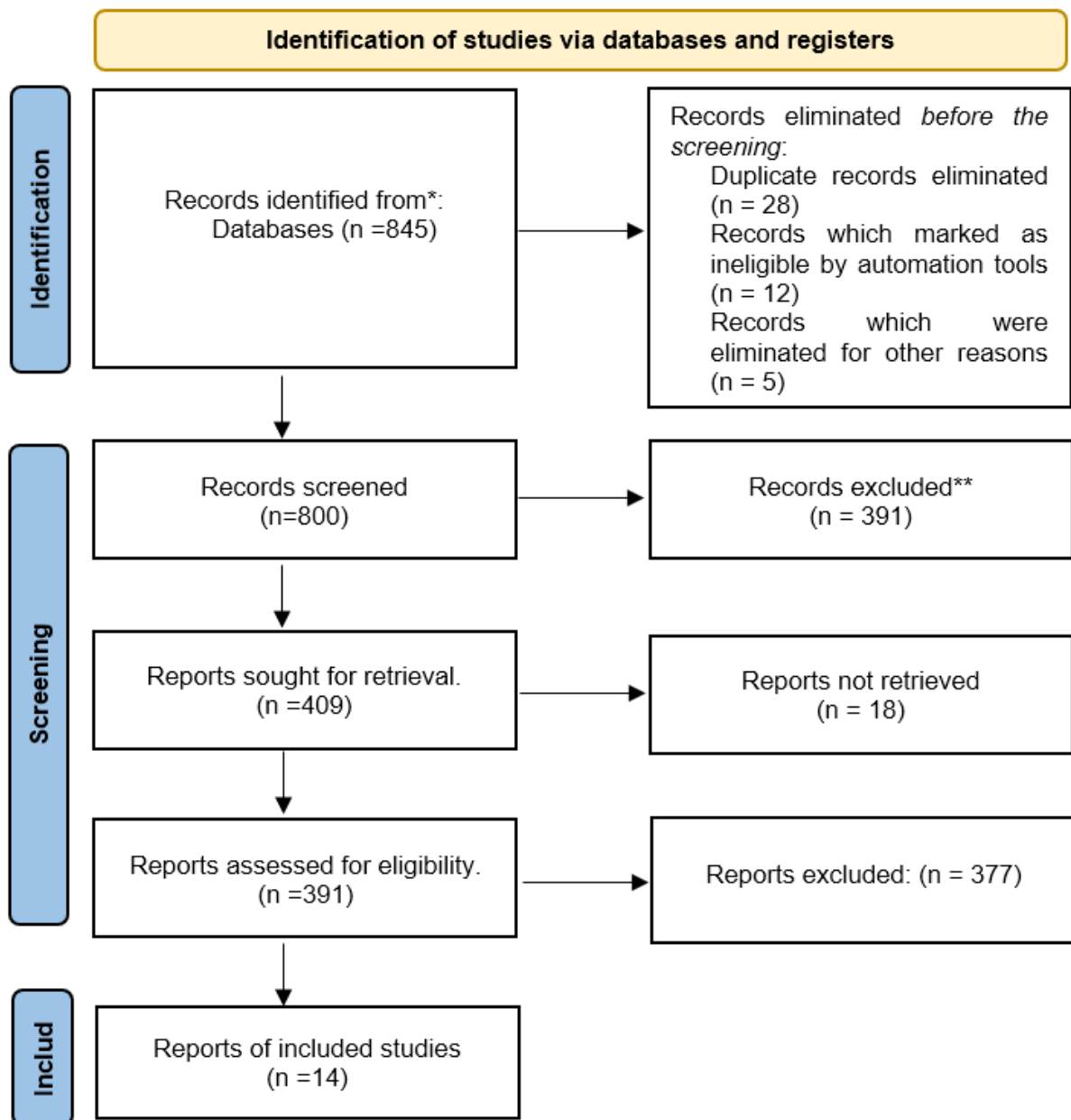


Figure 1: PRISMA 2020 flow diagram.

Table 1: Quality of the included studies.

Study. Years	Item													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Omar et al., 2022 ¹⁷	√	√	×	×	×	×	×	×	×	√	×	×	×	×
Yesildal et al., 2020 ¹⁸	√	√	√	√	√	√	×	×	×	√	√	√	×	×
Aboshama et al., 2021 ¹⁹	√	√	√	√	√	√	×	×	×	√	√	√	×	×
Karci et al., 2019 ²⁰	√	√	√	√	√	√	×	×	×	√	√	√	×	×
Hamad et al., 2018 ²¹	×	×	×	×	×	×	×	×	×	√	√	√	×	×
Jiangkongkho et al., 2018 ²²	×	×	×	×	×	×	×	×	×	√	√	√	×	×
Cevik et al., 2018 ²³	√	√	√	√	×	√	×	×	×	√	√	√	×	×
Salman et al., 2017 ²⁴	√	√	×	×	×	×	×	×	×	√	×	×	×	×
Alnamel et al., 2014 ²⁵	√	√	×	×	×	×	×	×	×	√	×	×	×	×
Tandra et al., 2018 ²⁶	√	√	×	×	×	×	×	×	×	√	×	×	×	×
Ahmed et al., 2016 ²⁷	√	√	√	√	×	√	×	×	×	√	√	√	×	×
Hamouda et al., 2014 ²⁸	√	√	√	√	×	√	×	×	×	√	√	√	×	×
Harini P et al., 2014 ²⁹	√	√	×	×	×	×	×	×	×	√	×	×	×	×
Nazirkar et al., 2014 ³⁰	√	√	√	√	×	√	×	×	×	√	√	√	×	×

Yes: √; No: ×

Table 2: Risk assessment.

Study. Years	Allocation concealment	Sample size	Blinding	Assessment methods	Selective outcome reporting	Risk of bias
Omar et al., 2022 ¹⁷	1	2	2	0	0	Moderate
Yesildal et al., 2020 ¹⁸	1	0	2	0	0	Low
Aboshama et al., 2021 ¹⁹	1	0	2	0	0	Low
Karci et al., 2019 ²⁰	1	0	2	0	0	Low
Hamad et al., 2018 ²¹	1	2	2	0	0	Moderate
Jiangkongkho et al., 2018 ²²	1	2	2	0	0	Moderate
Cevik et al., 2018 ²³	1	2	2	0	0	Moderate
Salman et al., 2017 ²⁴	1	2	2	0	0	Moderate
Alnamel et al., 2014 ²⁵	1	2	2	2	1	High
Tandra et al., 2018 ²⁶	1	0	2	0	0	Low
Ahmed et al., 2016 ²⁷	1	0	2	0	0	Low
Hamouda et al., 2014 ²⁸	1	2	2	0	0	Moderate
Harini P et al., 2014 ²⁹	1	2	2	2	1	High
Nazirkar et al., 2014 ³⁰	1	2	2	0	0	Moderate

Table 3: Review of selected studies and data collection (Al₂O₃).

Study. Years	Sample size (n)	Test Standard	Al ₂ O ₃ NPs				Fraction weight in %age
			Specimen size (mm ³)	Storage	Details (nm)	Dispersion Method	
Omar et al., 2022 ¹⁷	15	ISO	65 × 10 × 3	NR	NR	Laboratory experiments were conducted to select a mix that would achieve the best properties and prevent cracking.	1 (5)
							2 (5)
							3 (5)
Yesildal et al., 2020 ¹⁸	12	ISO 1567	65 × 10 × 3	at 37 °C for 8 h	10	The powder of acrylic resin is measured on balance with an accuracy of 1/10000 grams	1 (6)
							5 (6)
Aboshama et al., 2021 ¹⁹	15	ISO	65 × 10 × 2.5	NR	50	NR	1(5)
							2(5)
							3(5)
Karci et al., 2019 ²⁰	21	ISO 1567 standard	65 × 10 × 3.3	NR	15	Added to powder + Steel balls mixer	1(7)
							3 (7)
							5 (7)
Hamad et al., 2018 ²¹	20	ISO180	65 × 10 × 3.3	at 37 °C for 48 h	57.50	NR	1 (5)
							2(5)
							3(5)
							4(5)

Table 4: Review of selected studies and data collection (SiO₂).

Study. Years	Sample size (n)	Test Standard	SiO ₂ NPs				Fraction weight in %age
			Specimen size (mm ³)	Storage	Details (nm)	Dispersion Method	
Karci et al., 2019 ²⁰	21	ISO 1567 standard	65 × 10 × 3.3	NR	15	Added to powder + Steel balls mixer	1(7)
							3 (7)
							5 (7)
Jiangkongkho et al., 2018 ²²	16	ISO 20795-1:201319	65 × 10 × 3	50 ± 2 hours of immersion in 37°C deionized water	36	added to monomer + Rotor stator mixer	1 (8)
							5 (8)
Cevik et al., 2018 ²³	16	ISO 20795-1:(2013)	65x 10 x 3mm	NR	12	Added to monomer + Manual mixer	1 (8)
							5 (8)
Salman et al., 2017 ²⁴	30	ISO (20795 1:2008.32)	65x 10 x 2.5mm	At 37 °C for 14 days	50	Added to monomer + Ultrasonic mixer	3 (10)
							5 (10)
							7 (10)
Alnamel et al., 2014 ²⁵	30	ADA, 1999	65x 10 x 2.5mm	Immersed in distilled water for 48 hours	100	Added to monomer + Ultrasonic mixer	3 (10)
							5 (10)
							7 (10)

Table 5: Review of selected studies and data collection (TiO2).

Study. Years	Sample size (n)	Test Standard	TiO2 NPs				Fraction weight in %age (n)	Flexural strength
			Specimen size (mm)	Storage	Details (nm)	Dispersion Method		
Aboshama et al., 2021 ¹⁹	15	ISO	65 × 10 × 2.5	NR	50	NR	----	----
							1 (5)	----
							3 (5)	----
Karci et al., 2019 ²⁰	21	ISO 1567	65×10× 3	In distilled water for 30 days	13	Ball Milling	1 (7)	Increased
							3 (7)	Reduced
							5 (7)	Reduced
Tandra et al., 2018 ²⁶	18	ADA12	65×10× 2.5	at 37 °C for 48 h	NR	NR	1 (9)	Increased
							3 (9)	Reduced
Ahmed et al., 2016 ²⁷	10	ADA12	50×10× 3	NR	46	NR	1 (5)	Reduced
							5 (5)	Reduced
Hamouda et al., 2014 ²⁸	10	ADA12	65×10× 2.5	at 37 °C for 24 h	21	Add to resin powder and stir by hand	5 (10)	Reduced
Harini P et al., 2014 ²⁹	30	ISO 1567	65×10× 3	at 37 °C for 50 h	NR	Dispersion of TiO2 nanoparticles in monomers by ultrasonics	1 (10)	Increased
							2 (10)	Increased
							5 (10)	Increased
Nazirkar et al., 2014 ³⁰	30	ADA12	65×10× 3.3	50 hours in distilled water at 37 °C	7	added, then sonicated for one hour with the monomer	0.5 (15)	Reduced
							1 (15)	Reduced

Table 6: Review of selected studies and data collection (Zro2).

Study. Years	Sample size (n)	Test Standard	Zro2 NPs				Fraction weight in %age
			Specimen size (mm3)	Storage	Details (nm)	Dispersion Method	
Omar et al., 2022 ¹⁷	15	ISO	65 × 10 × 3	NR	NR	A laboratory test was used to select a mixture in order to achieve the best properties without forming cracks.	1 (5)
							2 (5)
							3 (5)
Aboshama et al., 2021 ¹⁹	21	PMMA without additive	65 × 10 × 2.5	NR	50	NR	1(7)
							2(7)
							3(7)

Meta-analysis

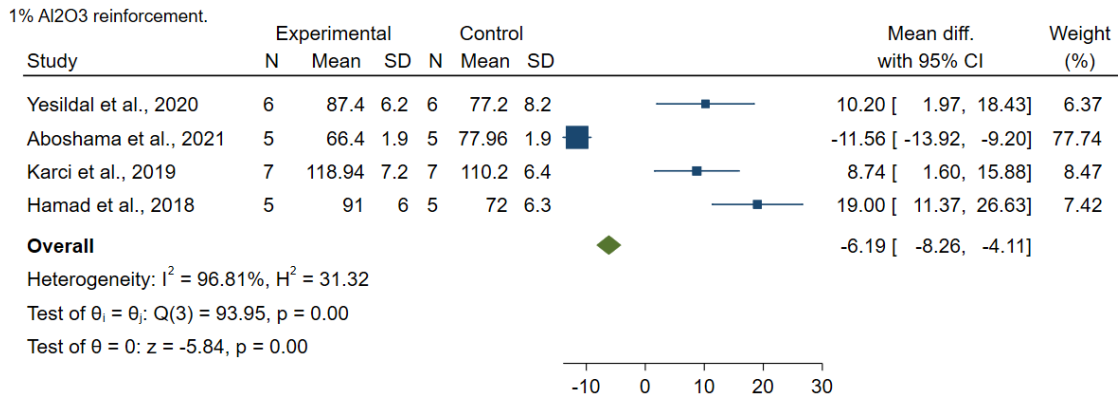
Aluminum oxide (Al₂O₃) nanoparticles:

Between the control group and the 1% Al₂O₃ reinforcement, there were -6.19 flexural strength mean differences (MD, -6.19 95% CI -8.26, -4.11; p=0.00) with high heterogeneity (I²=96.81%; P =0.00). This result showed that adding 1% Al₂O₃ nanoparticles significantly affects the flexural strength (p=0.00) (Figure 2).

Between the control group and the 5% Al₂O₃ reinforcement, there were -4.94 flexural strength

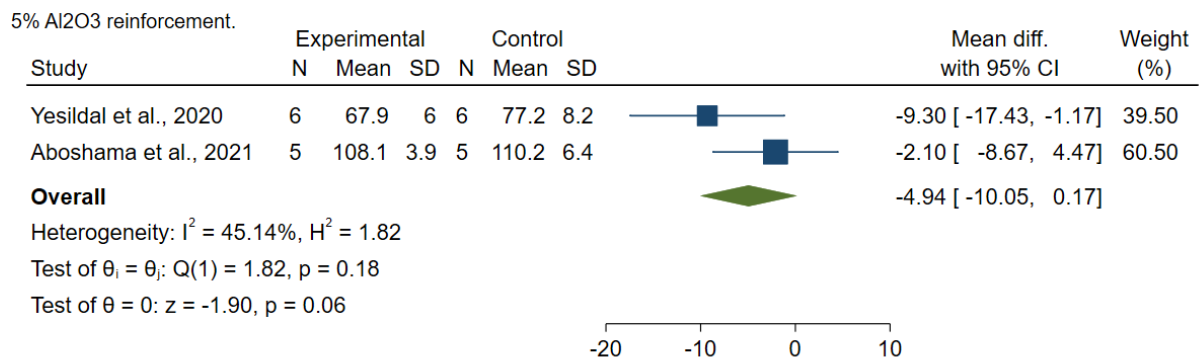
mean differences (MD, -4.94 95% CI -10.04, 0.17; p=0.06) with low heterogeneity (I²=45.14%; P =0.18). A significant effect of adding 5% Al₂O₃ nanoparticles on flexural strength was not observed (p=0.06) (Figure 3).

Between the control group and the 3% Al₂O₃ reinforcement, there were -14.76 flexural strength mean differences (MD, -14.76 95% CI -18.35, 11.18; p=0.00) with high heterogeneity (I²=97.32%; P =0.18). This result showed that adding 3% Al₂O₃ nanoparticles significantly affects the flexural strength (p=0.00) (Figure 4).



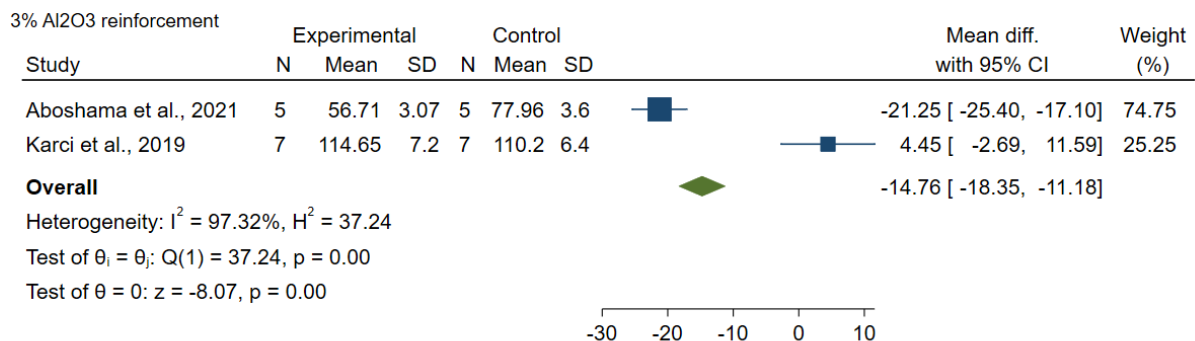
Fixed-effects inverse-variance model

Figure 2: The Forest plot displayed a mean difference in flexural strength of 1% Al₂O₃ reinforcement.



Fixed-effects inverse-variance model

Figure 3: The Forest plot displayed a mean difference in flexural strength of 5% Al₂O₃ reinforcement.



Fixed-effects inverse-variance model

Figure 4: The Forest plot displayed a mean difference of 2% Al₂O₃ reinforcement in flexural strength.

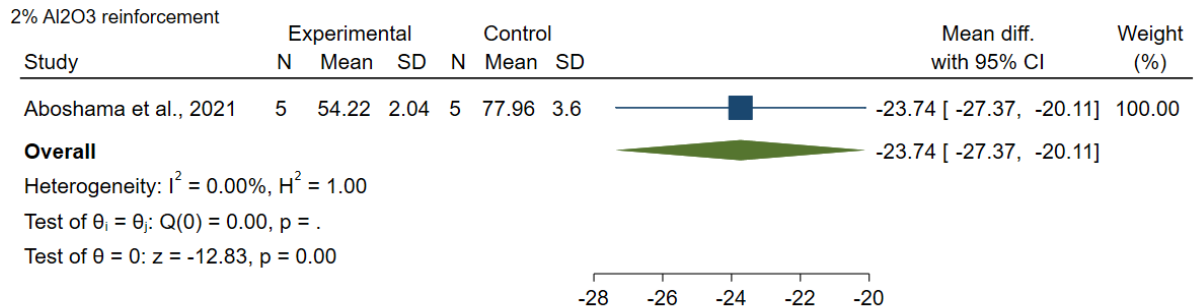
Between the control group and the 2% Al₂O₃ reinforcement, there were -23.74 flexural strength mean differences (MD, -23.74 95% CI -27.37, -20.11; p=0.00). This result showed that adding 2% Al₂O₃ nanoparticles significantly affects flexural strength (p=0.00) (Figure 5).

Silicon dioxide (SiO₂) nanoparticles

Between the control group and the 1% SiO₂ reinforcement, there were -58.74 flexural strength mean differences (MD, -58.74 95% CI -61.81, -55.68;

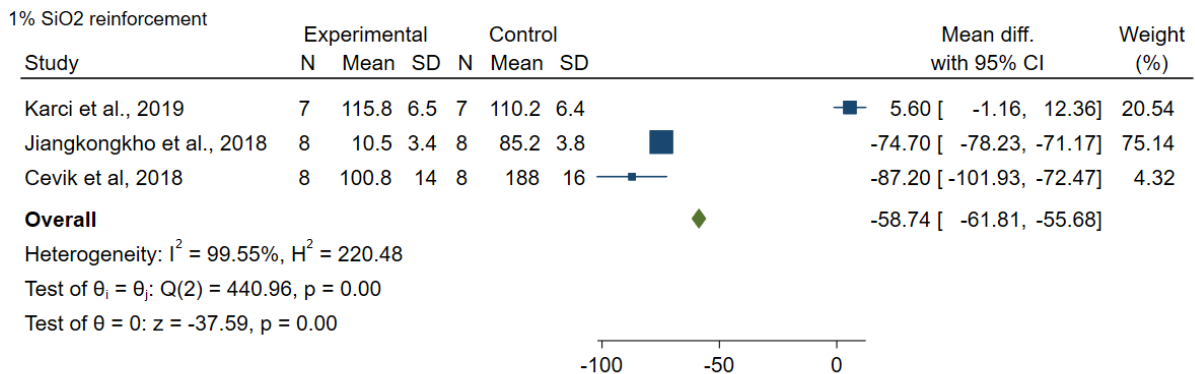
p=0.06) with high heterogeneity (I²=99.55%; P =0.00). This result showed that adding 1 % SiO₂ nanoparticles significantly affected flexural strength (p=0.00) (Figure 6).

Between the control group and the 3% SiO₂ reinforcement, there was 4.58 flexural strength mean differences (MD, 4.58 95% CI 3.61, 5.56; p=0.00) with much heterogeneity. (I²=95.17%; P =0.00). This result showed that adding 3 % SiO₂ nanoparticles significantly affected flexural strength (p=0.00) (Figure 7).



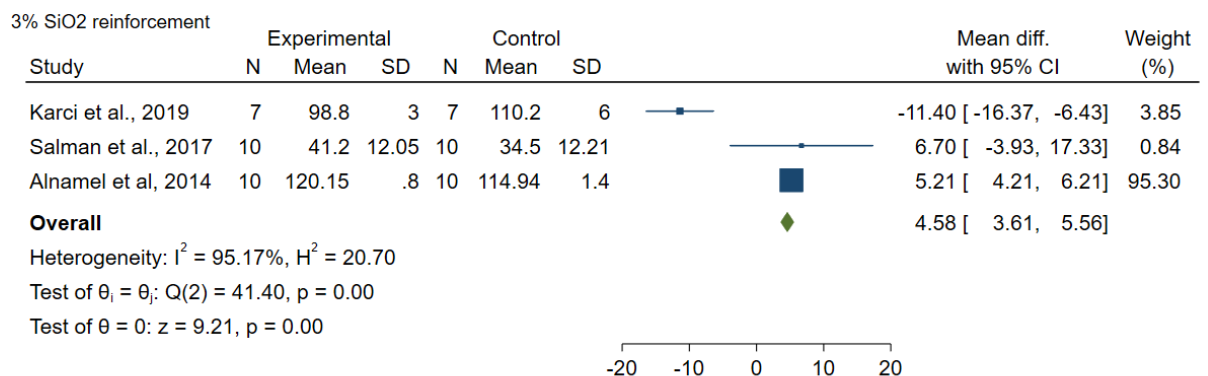
Fixed-effects inverse-variance model

Figure 5: The Forest plot displayed a mean difference in flexural strength of 2% Al₂O₃ reinforcement.



Fixed-effects inverse-variance model

Figure 6: The Forest plot displayed a mean difference in flexural strength of 1% SiO₂ reinforcement.



Fixed-effects inverse-variance model

Figure 7: The Forest plot displayed a mean difference in flexural strength of 3% SiO₂ reinforcement.

Between the control group and the 5% SiO₂ reinforcement, there was 7.74 flexural strength mean differences (MD, 7.74 95% CI 6.61, 8.87; p=0.00) with high heterogeneity (I²=99.50%; P =0.00). This result showed that adding 5 % SiO₂ nanoparticles significantly affected flexural strength (p=0.00) (Figure 8).

Titanium dioxide (TiO₂) nanoparticles

Between the control group and the 1% TiO₂ reinforcement, there were -4.08 flexural strength mean differences (MD, -4.08 95% CI -35.03, 26.87;

p=0.80) with low heterogeneity (I²=0%; P =0.97). A significant effect in flexural strength was not observed when 1% TiO₂ nanoparticles were added (p=0.80) (Figure 9).

Between the control group and the 3% TiO₂ reinforcement, there were -2.08 flexural strength mean differences (MD, -2.08 95% CI -5.62, 1.47; p=0.25) with low heterogeneity (I²=59.09%; P =0.12). As shown in figure 10, Flexural strength was unaffected by the addition of 3% TiO₂ nanoparticles (p=0.25).

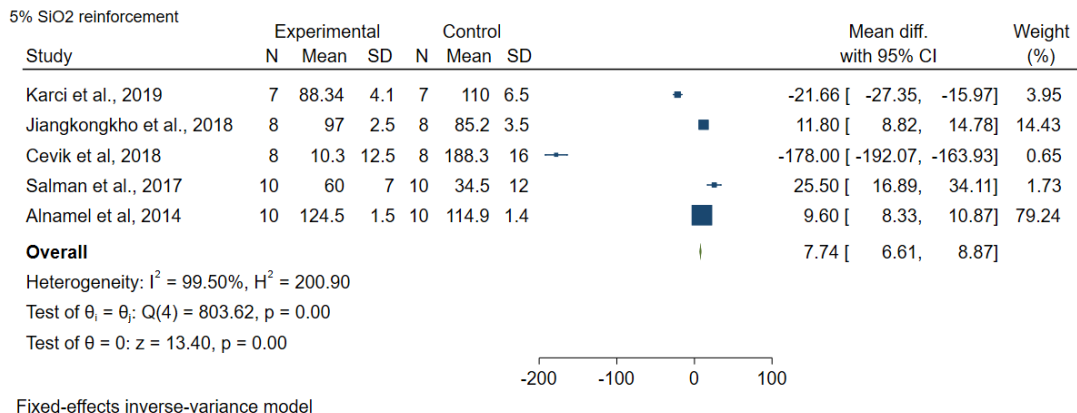


Figure 8: The Forest plot displayed a mean difference in flexural strength of 5% SiO₂ reinforcement.

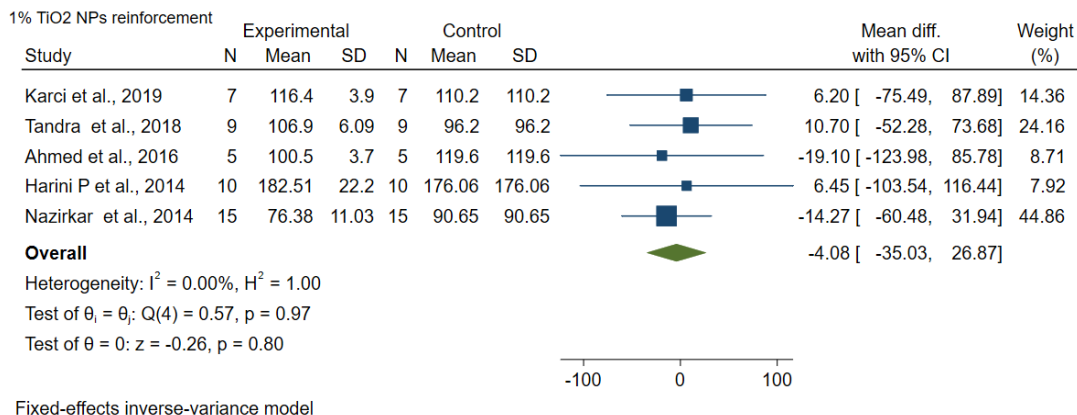


Figure 9: The Forest plot displayed a mean difference in flexural strength of 1% TiO₂ reinforcement.

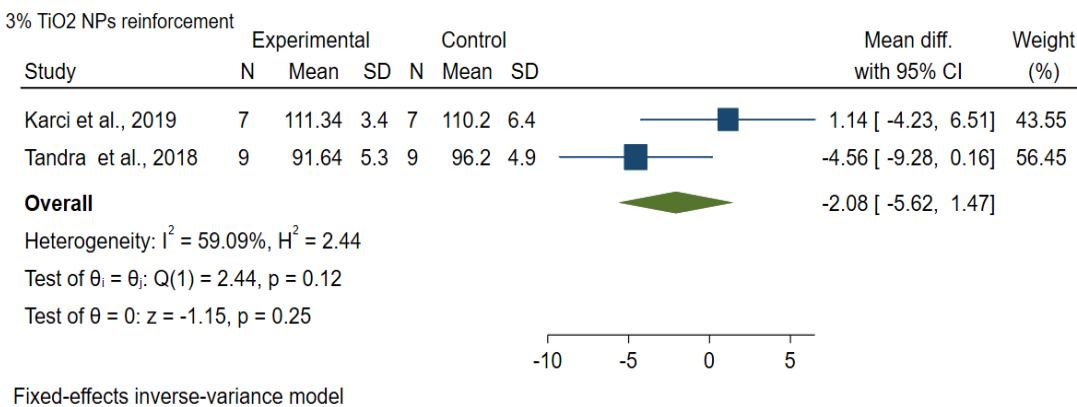


Figure 10: The Forest plot displayed a mean difference in flexural strength of 3% TiO₂ reinforcement.

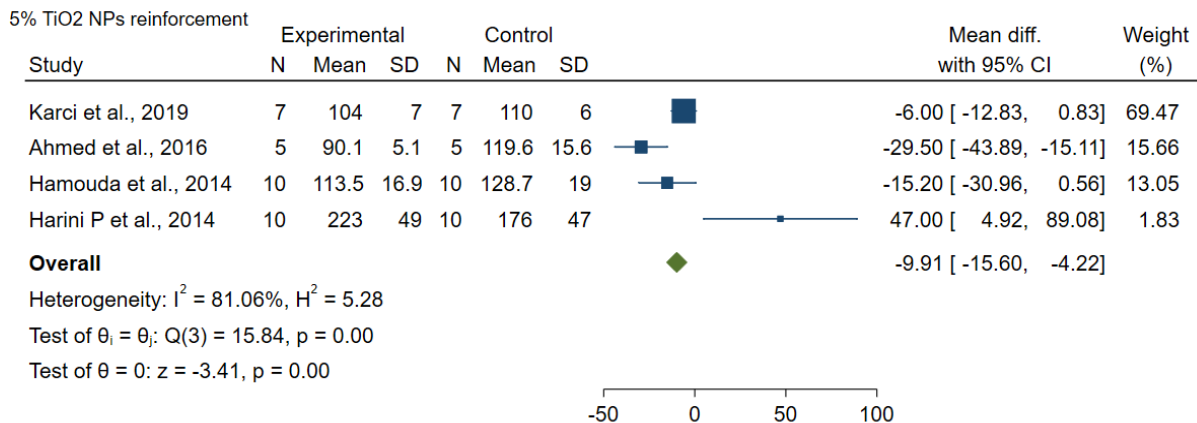
Between the control group and the 5% TiO₂ reinforcement, there were -9.91 flexural strength mean differences (MD, -9.91 95% CI -15.60, -4.22; p=0.00) with high heterogeneity (I²=81.06%; P =0.00). According to the experimental findings, 5 % TiO₂ nanoparticles significantly affected flexural strength (p=0.00) (Figure 11).

Zirconia (ZrO₂) nanoparticles

Between the control group and the 1% ZrO₂ reinforcement, there were -13.03 flexural strength

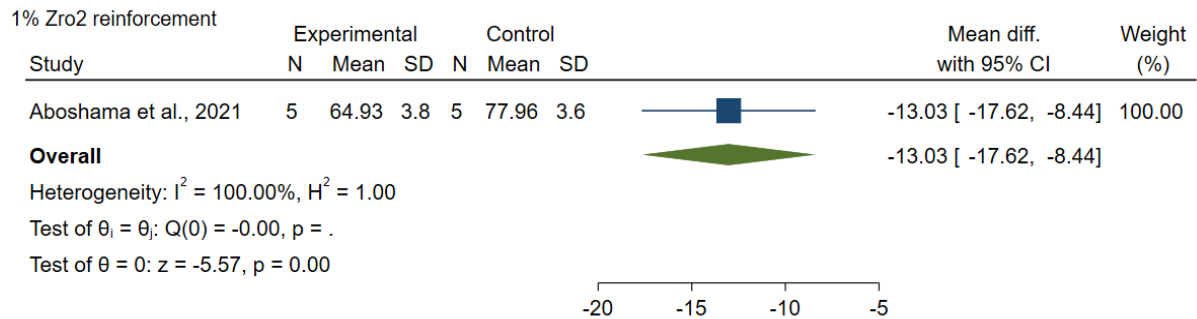
mean differences (MD, -13.03 95% CI -17.62, -8.44; p=0.00). This result showed that adding 1 % ZrO₂ nanoparticles significantly affected flexural strength (p=0.00) (Figure 12).

Between the control group and the 2% ZrO₂ reinforcement, there were -21.90 flexural strength mean differences (MD, -21.90 95% CI -27.88, -15.92; p=0.00). This result showed that adding 2 % ZrO₂ nanoparticles significantly affected flexural strength (p=0.00) (Figure 13).



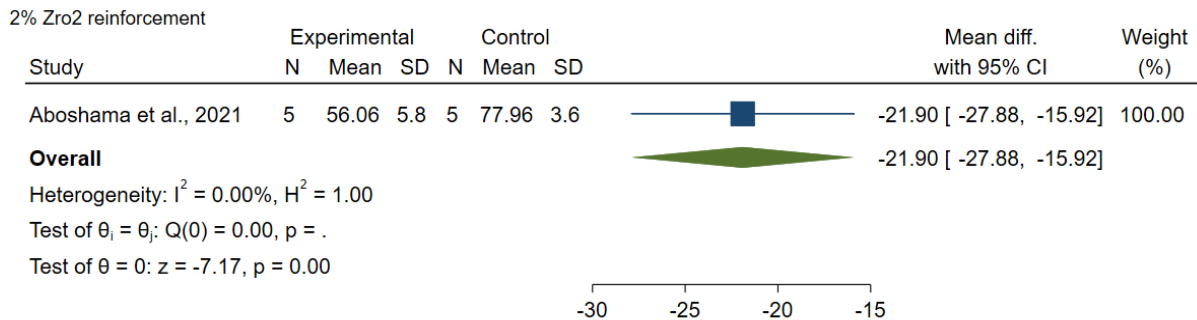
Fixed-effects inverse-variance model

Figure 11: The Forest plot displayed a mean difference in flexural strength of 5% TiO₂ reinforcement.



Fixed-effects inverse-variance model

Figure 12: The Forest plot displayed a mean difference in flexural strength of 1% ZrO₂ reinforcement.



Fixed-effects inverse-variance model

Figure 13: The Forest plot displayed a mean difference in flexural strength of 2% ZrO₂ reinforcement.

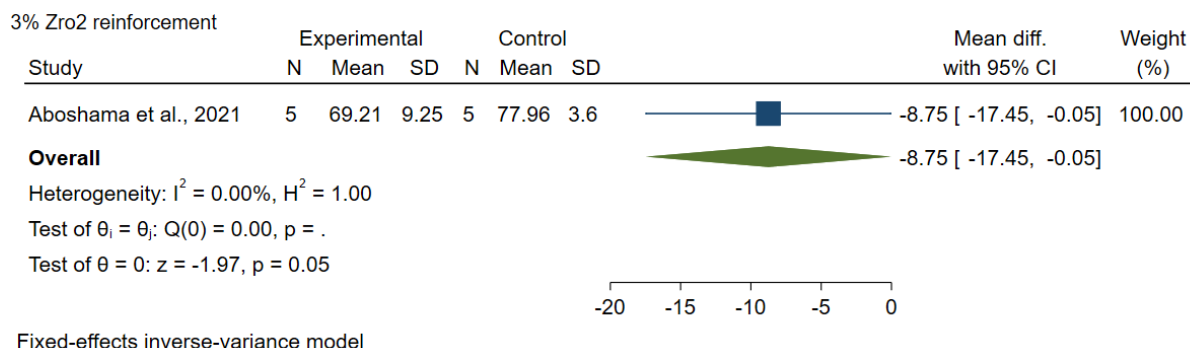


Figure 14: The Forest plot displayed a mean difference in flexural strength of 3% ZrO₂ reinforcement.

Between the control group and the 3% ZrO₂ reinforcement, there were -8.75 flexural strength mean differences (MD, -8.75 95% CI -17.45, -0.05; $p=0.05$). This result showed that adding 3% ZrO₂ nanoparticles significantly affected flexural strength ($p=0.05$) (Figure 14).

DISCUSSION

This investigation aims to evaluate the flexural strength of materials for dentures augmented with nanoparticles of Al₂O₃, SiO₂, TiO₂, and ZrO₂. Based on the findings of the current investigation, the flexural strength of the artificial tooth base material changes after adding nanoparticles. The size of filler particles and their form are two of the most significant elements that play a crucial role in enhancing the mechanical properties of polymer composites. Also, the filler percentage is very important. As the present meta-analysis showed, some nanoparticles can increase flexural strength in a lower percentage (refer to the result section). As a result of the present study, one reason for flexural strength improvements appears to be the low-concentration addition of nanoparticles due to the creation of a surface bond between the polymer matrix and the nanoparticles due to their homogeneous distribution within the matrix. Studies have also shown, in line with the current investigation's findings, the flexural strength of acrylic resin can be affected positively or negatively by different percentages of nanoparticles. Due to the high heterogeneity in some results, the results of the present study should be taken with caution. The high heterogeneity between studies can be related to the diversity in the research methodology because, in the studies, the test method, sample size, size and concentration of nanoparticles, composition, type of resin, and sample preparation were different. The high heterogeneity of the studies could also be due to the significant variation in the polymerization cycle. According to the present study's findings, an increase in flexural strength is observed in lower percentages, and higher ratios cause a decrease in flexural strength in some nanoparticles. Among the investigated nanoparticles, SiO₂ showed the

lowest density, which indicates its lower mechanical properties. Also, due to the very high ratio of surface area to the volume of TiO₂ nanoparticles, only a small amount is needed to change the properties of the polymer.^{31, 32} The fact that only flexural strength was investigated and analyzed in the current study and other mechanical properties were not constituted one of its limitations, so it is suggested that future studies examine other mechanical properties as well. A further limitation of the current study was that it did not investigate other criteria that may have contributed to the differences in the results other than bending strength. Also, another limitation is that only in vivo studies were investigated, which may differ from the laboratory environment due to oral conditions.

CONCLUSION

This study evaluated the flexural strength of artificial teeth base resin reinforced with various types of nanoparticles. Based on the current meta-analysis, it can be concluded that the properties of polymers reinforced with nanoparticles can depend on the type of nanoparticles and concentration. Different reports and results were observed between the selected studies, which could be due to disparity in polymerization cycles, testing and standardization techniques, and other factors. Based on the present study's findings, no specific concentration of Al₂O₃, SiO₂, TiO₂, or ZrO₂ nanoparticles can be reported as the most or least effective booster.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

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None declared.

AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	KY, NK
Acquisition, Analysis or Interpretation of Data:	KY, NK, AA, NG, FR, AA
Manuscript Writing & Approval:	KY, NK, AA, NG, FR, AA

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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