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REVIEW
PREGLEDNI RAD

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Antimicrobial and Mechanical Effects of Zeolite Use in Dental Materials: A Systematic Review

Antimikrobni i mehanički učinci upotrebe zeolita u dentalnim materijalima: sistematizirani pregledni rad

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Abstract

Objective: Ion-incorporated zeolite is a widely used antimicrobial material studied for various dental applications. At present, there is no other systematic review that evaluates the effectiveness of zeolite in all dental materials. The purpose of this study was to review all available literature that analyzed the antimicrobial effects and/or mechanical properties of zeolite as a restorative material in dentistry. **Material and methods:** Following PRISMA guidelines, an exhaustive search of PubMed, Ovid Medline, Scopus, Embase, and the Dentistry & Oral Sciences Source was conducted. No language or time restrictions were used and the study was conducted from June 1, 2020 to August 17, 2020. Only full text articles were selected that pertained to the usage of zeolite in dental materials including composite resin, bonding agents, cements, restorative root material, cavity base material, prosthesis, implants, and endodontics. **Results:** At the beginning of the study, 1534 studies were identified, of which 687 duplicate records were excluded. After screening for the title, abstract, and full texts, 35 articles remained and were included in the qualitative synthesis. An Inter-Rater Reliability (IRR) test, which included a percent user agreement and reliability percent, was conducted for each of the 35 articles chosen. **Conclusion:** Although ion-incorporated zeolite may enhance the antimicrobial properties of dental materials, the mechanical properties of some materials, such as MTA and acrylic resin, may be compromised. Therefore, since the decrease in mechanical properties depends on zeolite concentration in the restorative material, it is generally recommended to add 0.2-2% zeolite by weight.

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Introduction

Zeolite, an aluminosilicate with a tetrahedral crystalline structure, has extensive applications ranging from ecology to dentistry (1, 2). Zeolite is particularly useful to these fields due to its unique porous structure, which creates negatively charged channels and cavities that can hold cations, hydroxyl groups, and water molecules (1). Recently, zeolite's ability to uptake and release ions, combined with its superior biocompatibility and long-lasting effects, has increased the attention on the compound in dental research (2).

In addition to solely adding zeolite to materials, many studies in dentistry have attempted to combine zeolite with inorganic antimicrobial ions, such as silver and zinc, for controlled release (2). Particularly, most of the studies focus on silver-incorporated zeolite (AgZ) since zeolite has a strong affinity for silver ions. In addition, silver ions are less toxic to

Uvod

Zeolit, alumosilikat s tetraedrskom kristalnom strukturom ima široku primjenu – od ekologije do stomatologije (1, 2). Zeolit je posebno koristan za ta područja zbog jedinstvene porozne strukture koja stvara negativno nabijene kanale i šupljine u kojima se mogu naći kationi, hidroksilne skupine i molekule vode (1). Odnedavno se, zbog svojstva zeolita da apsorbira i oslobađa ione, u kombinaciji s njegovom odličnom biokompatibilnošću i dugotrajnim učincima, povećalo zanimanje za taj spoj u stomatološkim istraživanjima (2).

Uz dodavanje samo zeolita u materijale, u mnogim ga se istraživanjima pokušalo kombinirati s anorganskim antimikrobnim ionima poput srebra i cinka za kontrolirano otpuštanje (2). Autori većine istraživanja posebno se usredotočuju na zeolit sa srebrom (AgZ) jer zeolit ima jak afinitet prema ionima srebra. Uz to, ioni srebra manje su toksični za ljudska human tissues than other metallic ions, such as copper and mercury (3,4). When cations become available in the surrounding oral environment, zeolite exchanges the environmental cation with its embedded silver ions. This, in turn, only occurs with the presence of moisture and until the silver concentration meets the local equilibrium value. Therefore, AgZ may offer targeted and controlled release of antimicrobial ions in the oral microbiome (5).

Furthermore, ion-embedded zeolite may serve as a potential antimicrobial agent towards pathogenic oral microorganisms. When ions released from zeolite encounter specific oral microbes, it may hinder their development by causing the inactivation of key enzymes, interruption of RNA replication, and blockage of microbial respiration (5). Therefore, incorporation of cations into zeolite may potentially decrease oral bacterial growth when added to dental materials.

When zeolite is incorporated into dental materials for antimicrobial effect, it is also important to consider the effect on the mechanical properties of the material. Common activities such as mastication and speech exert forces on teeth and materials incorporated into dentition. Thus, it is critical to the efficacy of dental operations if the materials used can withstand these forces without compromising their strength. Properties imperative to the success of long-term dental operations include flexural strength, bond strength to tooth structure, compressive strength, setting time, and surface microhardness (6). If zeolite can be incorporated into dental materials without hindering their mechanical properties, there can be a potential reduction in oral infections while reducing failures of dental restorations.

In this systematic review, the antimicrobial and mechanical properties of zeolite in different branches of dentistry such as endodontics, prosthetics, implantology, and restorative dentistry are analyzed. Specifically, the available literature was reviewed to determine if adding silver (or zinc) zeolite to dental materials would increase the antimicrobial effectiveness without inhibiting the strength and hardness of materials. The aim of this systematic study was to review both *in vitro* and *in vivo* studies that evaluated the antimicrobial effects and mechanical properties of zeolite as a material in dentistry.

Material and Methods

Literature search strategy

An exhaustive search of PubMed, Ovid Medline, Scopus, Embase, and the Dentistry & Oral Sciences Source was conducted between June 1, 2020 and August 17, 2020. All published studies within the databases were screened for eligibility. There were no limitations set on the year or language of the publication. A controlled vocabulary was used (MeSH terms in Pubmed, Subject Headings in Ovid Medline, Emtree terms in Embase) across all databases as well as a search for free terms in the titles and abstracts. The grey literature search was conducted through ProQuest Dissertations & Theses Global and Trip Database. The searches through the electronic databases were separately completed by two authors (J.H. and S.L.). The following search terms were used: *MeSH terms:* "zeolites", "biomedical and dental materials",

tkiva od ostalih metalnih iona poput bakra i žive (3, 4). Kad kationi postanu dostupni u okolnom oralnom okružju, zeolit mijenja te katione za ugrađene ione srebra. To se, pak, događa samo uz prisutnost vlage i sve dok koncentracija srebra ne dostigne lokalnu vrijednost ravnoteže. Zato AgZ može osigurati ciljano i kontrolirano oslobađanje antimikrobnih iona u oralnom mikrobiomu (5).

Nadalje, zeolit s ugrađenim ionima može poslužiti kao antimikrobno sredstvo za patogene oralne mikroorganizme. Kada ioni oslobođeni iz zeolita naiđu na određene mikroorganizme iz oralnoga mikrobima, mogu otežati njihov razvoj i prouzročiti inaktivaciju ključnih enzima, prekid replikacije RNK i blokadu mikrobnoga disanja (5). Zato ugradnja kationa u zeolit može smanjiti rast oralnih bakterija ako se dodaju u dentalne materijale.

Kada se zeolit dodaje u dentalne materijale radi antimikrobnog učinka, također je važno uzeti u obzir učinak na mehanička svojstva materijala. Uobičajene aktivnosti, poput žvakanja i govora, čine silu na zube i dentalne materijale. Zato je presudno da upotrijebljeni materijali mogu podnijeti tu silu bez ugrožavanja integriteta. Svojstva nužna za dugoročni uspjeh nadomjestaka uključuju savojnu čvrstoću, veznu čvrstoću sa zubnom strukturom, tlačnu čvrstoću, vrijeme stvrdnjavanja i mikrotvrdoću površine (6). Ako se zeolit može ugraditi u dentalne materijale, a da se pritom ne poremete njihova mehanička svojstva, mogu se potencijalno smanjiti oralne infekcije, uz istodobno smanjenje oštećenja na zubnim nadomjestcima.

U ovom sistematiziranom preglednom radu analiziraju se antimikrobna i mehanička svojstva zeolita u različitim granama stomatologije, poput endodontskih zahvata, protetike, implantologije i restaurativne stomatologije. Točnije, pregledana je objavljena literatura kako bi se utvrdilo hoće li dodavanje zeolita sa srebrom (ili cinkom) dentalnim materijalima povećati antimikrobnu učinkovitost bez inhibiranja čvrstoće i tvrdoće materijala. Cilj ovog istraživanja bio je pregledati istraživanja *in vitro* i *in vivo* u kojima su autori procjenjivali antimikrobne učinke i mehanička svojstva zeolita kao materijala u stomatologiji.

Materijali i metode

Strategije pretraživanja literature

Ovaj sustavni pregled proveden je u skladu sa smjernicama PRISMA-e (Preferred Reporting Items for Systematic Reviews and Meta-Analyses – Preferirane stavke izvještavanja za sustavne pregledne radove i metaanalize), tablica 1.

Obavljena je iscrpna pretraga baza Pubmed, Ovid Medline, Scopus, Embase te Dentistry i Oral Sciences Source između 1. lipnja i 17. kolovoza 2020. Sva objavljena istraživanja u bazama podataka provjerena su kako bi se utvrdilo ispunjavaju li uvjete za uključivanje. Nisu postavljena ograničenja za godinu ili jezik izdanja. U svim bazama podataka korišten je kontrolirani rječnik (MeSH u Pubmedu, Subject Headings u Ovid Medlineu, Emtree terms u Embaseu) te slobodni pojmovi u naslovima i sažetcima. Pretraživanje sive literature provedeno je u bazi ProQuest Dissertations i Theses "dental cavity lining", "resin cements", "dental cements", "dental restoration, permanent", "dental restoration, temporary", "composite resins", "ceramics", "dental porcelain", "dental veneers", "dentures", "acrylic resin"; *Subject Headings:* "dental cements", "dental cavity lining", "resin cements", "dental restoration, permanent"; "composite resin", "ceramics", "dental porcelain", "dental veneers", "dentures", "acrylic resin"; *Emtree Terms:* "dental materials", "resin cement", "dental restoration", "dentures", "dental porcelain", "dental veneers", "composite resin", "dental prosthesis and implant", "biomedical and dental materials." *Free Terms:* zeolite, clinoptilolite, dental materials, dental cements, dental restoration, dental base material, dental liners, dental ceramics, dental porcelain, dental veneers, dentures, dental acrylic resin.

Eligibility Criteria

Studies that pertained to the usage of zeolite in dental materials such as composite resin, bonding agents, cements, restorative root material, cavity base material, prosthesis, implants, and endodontics were included in this systematic review. In addition, only full texts were selected for inclusion. Zeolite used in oral rinses or oral medicaments was excluded as well as those studies pertaining to tissue conditioners. Literature reviews and abstracts were excluded to meet the full-text-only eligibility criteria.

Screening and Selection

The studies that were collected were screened independently by two researchers (J.H. and S.L.) for titles and abstracts that met the identified inclusion criteria. Differences in opinions were discussed between the two researchers until a consensus was reached. Following the discussion, the two reviewers separately screened the selected full texts for eligibility. Disagreements were discussed until a consensus was reached. Due to the COVID-19 pandemic, the numbers of active libraries were smaller than normal. Therefore, with all resources exhausted, the full texts of 3 chosen articles were still unable to be procured and included in the analysis portion of the systematic review. At last, the references of the selected articles were reviewed, and eligibility was determined based on the inclusion criteria. Disagreements were resolved between the two reviewers and discussions with a mentor (F.O.).

Data Extraction

Prior to data extraction, a protocol was agreed upon by two of the authors (J.H. and S.L.). Data were then extracted from the selected full text articles and organized on an excel sheet. The two authors extracted the data including authors, publication year, type of study, antimicrobial/mechanical properties, sample size, materials used, results, microbes tested, and risk of bias, Table 1, Table 2.

Assessment of Risk of Bias of Reviewed Papers

For *in vitro* studies and randomized control trials, the risk of bias assessment was considered based on a previous study

Global and Trip Database. Pretrage elektroničkih baza podataka odvojeno su provela dva autora (J. H. i S. L.). Korišteni su sljedeći pojmovi za pretraživanje: MeSH pojmovi: *zeolit, biomedicinski i dentalni materijali, kavitetne podloge, smolasti cementi, zubni cementi, zubna restauracija – trajna, zubna restauracija – privremena, kompozitne smole, keramika, dentalna keramika, zubne ljuske, proteze, akrilatna smola*; Subject Headingd: *zubni cementi, kavitetne podloge, smolasti cementi, zubna restauracija – trajna; kompozitna smola, keramika, dentalna keramika, zubne ljuske, proteze, akrilatna smola*; Emtree terms: *dentalni materijali, smolasti cement, zubna restauracija, proteze, dentalna keramika, zubne ljuske, kompozitna smola, zubna proteza i implantat, biomedicinski i dentalni materijali*. Slobodni pojmovi: *zeolit, klinoptilolit, dentalni materijali, dentalni cementi, restauracija zuba, materijal za podloge, kavitetne podloge, dentalna keramika, zubne ljuske, proteze, akrilatna smola*, tablica 2.

Kriteriji prihvatljivosti

Istraživanja koja su se odnosila na upotrebu zeolita u dentalnim materijalima kao što su kompozitne smole, adhezivi, cementi, korijenski materijali, kavitetne podloge, materijali za protetiku, implantologiju i endodoncija uključena su u ovaj sistematizirani pregled. Odabrani su samo cjeloviti tekstovi. Izuzeti su zeoliti koji se upotrebljavaju u oralnim otopinama za ispiranje ili za oralne lijekove te oni koji se primjenjuju u regeneraciji tkiva. Recenzije literature i sažetci su izuzeti.

Pregled i odabir

Dva istraživača (J. H. i S. L.) neovisno su pregledala prikupljena istraživanja prema naslovima i sažetcima koji su zadovoljili utvrđene kriterije za uključivanje. U slučaju neslaganja razgovarali su o razlikama u mišljenju dok nisu postigli konsenzus. Nakon završene rasprave dva recenzenta odvojeno su pregledala odabrane cjelovite tekstove kako bi ustanovili ispunjavaju li uvjete. O nesuglasicama su raspravljali dok nije postignut konsenzus. Zbog pandemije virusa COVID-19 broj knjižnica koje rade bio je manji od uobičajenoga. Stoga, nakon što su svi resursi iscrpljeni, cjeloviti tekstovi triju odabranih radova nisu bili dostupni te se nisu mogli uključiti u dio o analizi ovoga sustavnoga preglednog rada. Na kraju je pregledana literatura odabranih radova i utvrđena je prihvatljivost na temelju kriterija za uključivanje. Riješene su nesuglasice između dvaju recenzenata i obavljen je razgovor s mentorom (F. O.).

Vađenje podataka

Prije vađenja podataka, dva autora (J. H. i S. L.) dogovorila su protokol. Podatci su zatim izvučeni iz odabranih radova s cjelovitim tekstom i organizirani na Excel tablici. Zatim su izdvojeni podatci, uključujući autore, godinu izdanja, vrstu istraživanja, antimikrobna/mehanička svojstva, veličinu uzorka, upotrijebljene materijale, rezultate, testirane mikrobe i rizik od pristranosti, tablica 1, tablica 2.

Procjena rizika od pristranosti pregledanih radova

Za randomizirana kontrolirana istraživanja *in vitro* provedena je procjena rizika od pristranosti na temelju prethodnog

(7), and each study was assessed on the basis of the following five parameters: I) sample size, II) presence of control, III) blinding of the operator, IV) standardized sample preparation, and V) single operator.

For each parameter I-IV, a score of 0 was given to an article if the criteria were reported clearly, a score of 1 was given to an article if the criteria were vague or insufficiently reported, and a score of 2 was given to an article if the information was not present. For parameter V, a score of 0 was given to an article if there was one operator, a score of 1 was given to an article if there were more operators, and a score of 2 was given to an article if the information was not present.

The five parameter scores for each article were then added for a cumulative score. Articles that were at low risk of bias scored between 0-3, moderate risk of bias scored between 4-7, and high risk of bias scored between 8-10. Two authors (J.H. and S.L.) independently assessed the risk of bias criteria for each article in duplicate, and any disagreements during the evaluation were later discussed and a consensus was reached.

Inter-Rater Reliability (IRR)

An Inter-Rater Reliability (IRR) test within the risk of bias test was conducted using a kappa calculator. Percent user agreement was calculated by taking the number of studies given the same risk of bias scores by both authors and dividing it by the total number of studies. The same risks of bias scores were considered in order to use the Cohen's Kappa test (8), and the resulting kappa values are reported, Table 2. To obtain the percent data that are reliable, the kappa values were squared. From these percentages, a level of agreement was described for each parameter (8).

Results

Search and Selection

The selection process is summarized in the Prisma Flow Chart shown in Figure 1 following Moher et al. (9). A database, grey literature, and reference search yielded 1534 studies, of which 687 duplicate records were excluded. The remaining 847 records were screened for title and abstract, and 801 were removed since they did not meet the eligibility criteria. 46 remaining articles were assessed for eligibility by examining the full-texts, and 11 articles did not meet the eligibility criteria and were therefore excluded. Of the remaining 35 articles included in the qualitative synthesis, 17 studied antimicrobial effects, 12 studied mechanical properties, and 6 studied both properties, Table 1.

Risk of Bias Test of the Studies in the Systematic Review

Supplementary [S3 Table] shows the risk of bias data of the 35 articles analyzed following the methods outlined by Astudillo-Rubio et al. (7). As shown in the table, the majority of papers were given a score of 2 by both authors in the "blinding operator" and "single operator" parameters for failing to provide any pertinent information. All studies had a moderate risk of bias except three studies with low, and one study with high risk of bias (9-15). The study with a high risk of bias score failed to use a control and did not reveal any

istraživanja (7), a svaki rad procijenjen je na temelju sljedećih pet parametara: 1) veličine uzorka, 2) prisutnosti kontrole, 3) zasljepljivanja istraživača, 4) standardizirane pripreme uzoraka i 5) broja ocjenjivača.

Za svaki parametar od 1 do 4 istraživanje je dobilo ocjenu 0 ako su kriteriji jasno navedeni, 1 ako je kriterij bio nejasan ili nedovoljno objašnjen, a ocjenu 2 ako informacija nije bilo. Za parametar 5 rad je dobio ocjenu 0 ako postoji jedan procjenitelj, ocjenu 1 ako je u radu bilo više od jednog procjenitelja, a ocjenu 2 ako podatci o broju procjenitelja nisu navedeni.

Tada su za svaki rad zbrojene ocjene za svaki parametar da bi se dobio kumulativni rezultat. Radovi s malim rizikom od pristranosti postigli su ocjenu od 0 do 3, umjereni rizik od pristranosti ocjenu od 4 do 7 i visoki rizik od pristranosti ocjenu od 8 do 10. Dva su autora (J. H. i S. L.) neovisno procjenjivala rizik kriterija pristranosti za svaki rad, a poslije su tijekom procjene raspravljali o svim neslaganjima dok nisu postigli konsenzus.

Pouzdanost među ocjenjivačima (IRR)

Test pouzdanosti među ocjenjivačima (IRR), u sklopu procjene rizika od pristranosti, proveden je Kappa testom. Postotak podudaranja izračunat je uzimajući broj istraživanja s jednakim rizikom od pristranosti obaju autora i dijeleći ga s ukupnim brojem istraživanja. Jednaki rizik od pristranosti korišten je za provođenje Cohenova Kappa testa (8), a dobiveni rezultati prikazani su u tablici 2. Da bi se dobili pouzdani podatci o postotku, Kappa vrijednosti su pomnožene na kvadrat. Iz tih postotaka opisana je razina podudaranja za svaki parametar (8).

Rezultati

Pretraživanje i odabir

Proces odabira sažet je u dijagramu PRISMA prikazanom na slici 1., prema Moheru i suradnicima (9). U bazama podataka, sivoj literaturi i pretraživanjem referencija pronađena su 1534 istraživanja od kojih je 687 dvostrukih zapisa isključeno. Preostalih 847 pregledano je prema naslovu i sažetku, a 801 je izbačen jer nisu zadovoljavali kriterije. Preostalih 46 radova ocijenjeno je nakon što su pregledani cjeloviti tekstovi kako bi se ustanovilo ispunjavaju li uvjete, a 11 radova nije zadovoljavalo kriterije prihvatljivosti te su isključeni. Od preostalih 35 radova uključenih u kvalitativnu sintezu, autori 17 njih proučavali su antimikrobne učinke, 12 mehanička svojstva, a 6 oba svojstva, tablica 1.

Testiranje rizika od pristranosti istraživanja iz sistematiziranog pregleda

Sva istraživanja imala su umjereni rizik od pristranosti, osim triju s niskim i jednim istraživanjem s visokim rizikom od pristranosti (9-15). U istraživanju s visokim rizikom od pristranosti nije bilo kontrole i nisu otkriveni nikakvi podatci o ocjenitelju. Nadalje, oba su autora podatke o veličini uzorka i standardiziranoj pripremi uzorka smatrali nejasnima. No rad se uklapao u kriterije za uključivanje koje su odredili autori pa je uključen kako se ne bi uskratile nikakve relevantne informacije.

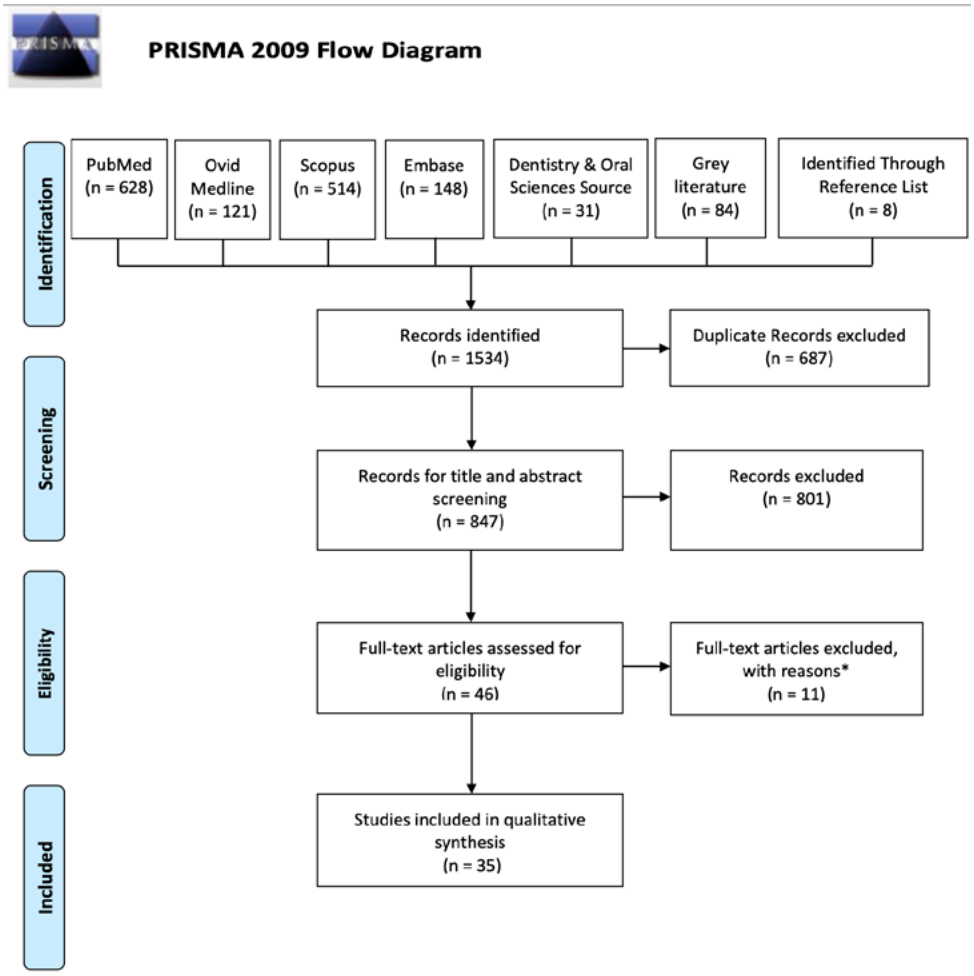

Figure 1 The Prisma Flow Diagram
*: 2 studied remineralizing potential, 1 studied biocompatibility, 2 studied color stability, 1 studied porosity, 1 studied surface roughness, 3 were unable to be accessed due to COVID-19 library closures, 1 unable to be accessed in English.
For more information on the PRISMA Flow Chart, visit www.prisma-statement.org.

Slika 1. Prisma dijagram
*: dva su proučavala remineralizacijski potencijal, jedan biokompatibilnost, dva stabilnost boje, jedan poroznost, jedan hrapavost površine, trima nije bilo moguće pristupiti zbog zatvaranja knjižnice zbog virusa COVID-19, jednomu nije bilo moguće pristupiti na engleskom jeziku.
Za više informacija o PRISMA dijagramu posjetite www.prisma-statement.org.

information about the operator. Furthermore, information about sample size and standardized sample preparation were considered vague by both authors. However, the paper met the inclusion criteria considered by the authors; hence it was included in order not to withhold any relevant information.

Inter-rater Reliability Results

The results of IRR tests for each risk of bias parameter are shown in Table 2. All parameters showed at least 74% or higher in percent user agreement and the average percent user agreement across all five parameters was 89.06%. The average percent of data that are reliable, as determined by Cohen's Kappa Test, is 46.6%, indicating an overall moderate level of reliability. Because the risk of bias test included 3 different possible scores, the discrepancies between authors were due to whether the parameters in question were clearly specified in the studies. Therefore, most of the score differences were due to one author judging an article as clearly reporting the parameter, while the other author judged the article

Rezultati pouzdanosti između ocjenjivača

Rezultati IRR testova za svaki parametar rizika od pristranosti prikazani su u tablici 2. U svim je parametrima postignut postotak od najmanje 74 % ili podudarnost među ocjenjivačima, a prosječni postotak podudarnosti u svih pet parametara bio je 89,06 %. Prosječni postotak pouzdanih podataka, kako je utvrđeno Cohenovim Kappa testom, iznosio je 46,6 %, što upućuje na ukupno umjerenu razinu pouzdanosti. Budući da je test pristranosti obuhvaćao tri različita moguća rezultata, neslaganja između ocjenjivača nastala su ovisno o tomu jesu li parametri jasno navedeni u istraživanjima. Zato je većina razlika nastala zato što je jedan autor ocijenio da se u radu jasno navodi traženi parametar, a drugi je

Table 1 Summary of the studies included in the systematic review
Tablica 1. Sažetak istraživanja uključenih u sistematizirani pregledni rad

Author, Year • Autor, godina	Type of Study • Vrsta istraživanja	Property • Svojstvo	n	Materials Used • Korišteni materijali	Results • Rezultati	*Microbes Tested • Testirani mikrobi*
Saengmee-Anupharb et al [10] (2013)	*In vitro*	A	3 per group	AgZ, AgZrPSi, AgZrP	All inorganic materials with silver had antimicrobial effects.	*S. mutans, L. casei, C. albicans, S. aureus*
Cinar et al [14] (2008)	*In vitro*	A	5 per material	GIC (Endion), AgZ	AgZ increased the antimicrobial effects	*S. milleri, S. aureus, E. faecalis*
Can-Karabulut et al [21] (2010)	*In vitro*	M	10 per material	GIC, zeolite, bone hydroxyapatite, provisional cement	Bond strength decreased with zeolite in cement.	N/A
Chung et al [20] (2001)	RCT	M	10 per subgroup	Ketac-Endo, KT-308, ZUT	ZUT and KT-308 showed highest bond strength.	N/A
Ghatole et al [28] (2016)	*In vitro*	A	3 per group	MTA, AgZ, CHX	MTA with AgZ showed the greatest efficacy against *E. faecalis*.	*E. faecalis*
Ghivari et al [25] (2017)	*In vitro*	A	5 per material	Na Hypochlorite, Octenidine, AgZ	AgZ showed the least antimicrobial effectiveness.	*E. faecalis, S. aureus, C. albicans*
Hotta et al [3] (1998)	*In vitro*	B	6 per group	Ag-Zn-Zeolite, SiO2 filler and urethane acrylate paste	Ag-Zn-Ze inhibited *S. mutans* and *S. mitis* but not *S. salivarius* or *S. sanguis*.	*S. mutans, S. mitis, S. salivarius, S. sanguis*
Kawahara et al [4] (2000)	*In vitro*	A	6 per group	Zeomic, AgZ	AgZ inhibited microbial growth under anaerobic conditions.	*P. gingivalis actinomycetemcomitans, S. mutans, A. viscosus, S. aureus*
Kim et al [16] (2016)	*In vitro*	B	N/S	CHX-loaded zeolite nanoparticles, GIC	GIC + CHX/Zeolite inhibited *S. mutans*. No decrease in compressive or bond strength	*S. mutans*
Kuroki et al [37] (2010)	*In vitro*	A	6 per material	self-cured acrylic resin (UNIFAST III), zeomic, bactekiller, novaron	Adding zeomic decreased *S. mutans*	*S. mutans*
Lee et al [13] (2007)	*In vitro*	B	N/S	Zeomic, GIC	Zeomic improved antimicrobial properties. Below 3% wt retained compressive strength.	*S. mutans*
Li et al [23] (2020)	RCT	A	N/S	EMT nano-zeolites, silver ions, dental adhesive (ASB2)	Inhibited biofilm growth/ attachment.	*S. mutans, S. gordonii, S. sanguinis*
Mabrouk et al [15] (2013)	*In vitro*	A	N/S	ZnZ, AgZ, GIC	Adding ZnZ or AgZ to GIC inhibited bacteria.	*B. subtilis, C. albicans, E. coli, S. aureus*
Padachey et al [18] (2000)	*In vitro*	A	10 per group	GIC, gutta percha, ZUT	ZUT was not more effective than GIC. But gutta percha improved the resistance to bacterial ingress.	*E. faecalis*
Partoazar et al [11] (2019)	*In vitro*	A	N/S	nano-ZnO zeolite, ZnO zeolite	NanoZnO/zeolite was effective in inhibiting *E. faecalis* biofilm	*E. faecalis*
Cinar et al [29] (2013)	*In vitro*	M	3 per material	MTA powder, AgZ	Adding AgZ to MTA didn't decrease physio-chemical properties.	N/A
El-Guindy et al [24] (2010)	*In vitro*	M	30 per group, 10 per subgroup	Rely X Unicem, G bond, ZnZ	Pretreatment of dentin with G bond and ZnZ increased bond strength between dentin/alloy.	N/A
Ghasemi et al [30] (2019)	*In vitro*	M	20 per group	MTA powder, 2% Ag-Zn-Ze composite	MTA with 2% Ag-Zn-Ze decreased push-out bond strength.	N/A
Ghatole et al [26] (2016)	*In vitro*	A	4 per group	Calcium hydroxide, AgZ, 2% CHX	AgZ in calcium hydroxide increased antimicrobial activity	*E. faecalis*
Casemiro et al [40] (2008)	*In vitro*	B	10 per group	Microwave-polymerized acrylic resin, Heat-polymerized resins, AgZ	Acrylic resin with Ag-Zn-Ze increased antimicrobial effects.	*C. albicans and S. mutans*
Malic et al [38] (2019)	*In vitro*	A	6 per group	Dental acrylics, AgZ, Na-zeolite	Adding zeolite to dental acrylics increased antimicrobial effect.	*S. mutans, F. nucleatum, C. albicans*

Odabas et al [27] (2011)	*In vitro*	A	5 per group	AgZ, MTA	MTA with zeolite increased antimicrobial effects except against *P. intermedia* and *A. israelii*.	*S. aureus, E. faecalis, E. coli,* *, C. albicans, P. gingivalis, C. A. israelii, P. intermedia*
Patel et al [17] (2000)	*In vitro*	A	108 per group	KT-308, Zeomic	Regardless of concentration, all ZUT inhibited *E. faecalis* at 15 hours.	*E. Faecalis*
Sandomierski et al [22] (2019)	*In vitro*	M	10 per material	Zeolite filler, diazonium cation methacrylic resin-based composite	Diazonium-modified zeolite fillers improved compressive and flexural strength.	N/A
Saravanan et al [32] (2015)	*In vitro*	A	30 patients	AgZ, soft liners	Soft liner with AgZ inhibited bacterial growth	*c. albicans,* gram negative bacteria
Tamanai-Shacoor et al [12] (2014)	*In vitro*	B	3 per group	AgZ, ASCOP	AgZ with ASCOP inhibited *P. gingivalis* but not *S. gordonii* growth.	*P. gingivalis, S. gordonii*
Naji et al [34] (2017)	*In vitro*	M	10 per group	Sodalite, alumina, ZTA, glass	Sodalite-infiltrated ceramics had higher shear bond strength than glass-infiltrated.	N/A
Naji et al [35] (2018)	*In vitro*	M	20 per group	KBr-Sodalite, porous alumina, ZTA	Increasing sintering temp of SOD-ZTA/A increased hardness and bond strength.	N/A
Naji et al [33] (2016)	*In vitro*	M	10 per group	sodalite, zeolite-infiltrated alumina (IA-SOD), ZTA, glass	Sodalite-infiltrated ZTA had increased fracture toughness.	N/A
Naji et al [36] (2016)	*In vitro*	M	10 per group	Sodalite, alumina, ZTA, glass	Sodalite infiltrated alumina and ZTA were in the acceptable range of hardness and flexural strength.	N/A
Yadav et al [41] (2015)	*In vitro*	M	10 per group	Fluconazole, CHX Gluconate, Ag-Zn-Ze, PMMA	Flexural strength decreased significantly	N/A
Nakanoda et al [39] (1995)	*In vitro*	B	4 per group	Zeomic, acrylic resin	Tensile and bending strength decreased in zeolite containing resin,	*C. albicans*
Samiei et al [31] (2017)	*In vitro*	M	15 per group	MTA, 2% Ag-Zn-Ze	Mixing MTA with 2% Ze-Ag-Zn decreased compressive strength.	N/A
Wang et al [42] (2011)	*In vitro*	A	3 per material	Titanium alloy, AgZ, ZTA, AgZ titanium alloy	Zeolite coating on implant reduced bacterial growth	*S. aureus*
McDougall et al [19] (1999)	*In vitro*	A	10 per group	ZUT, Kerr sealer, KT-308, gutta percha	*E. faecalis* penetration increased in canals filled with ZUT	E. faecalis

Abbreviations: N/S: Not Stated; N/A: Not Applicable; A: Antimicrobial; M: Mechanical; B: Both Antimicrobial and Mechanical; PMMA: Polymethylmethacrylate; ZTA: Zirconium Toughened Alumina; AgZ: Silver-Incorporated Zeolite; ZnZ: Zinc-Incorporated Zeolite; Ag-Zn-Ze: Silver-Zinc-Incorporated Zeolite; MTA: Mineral Trioxide Aggregate; GIC: Glass Ionomer Cement;
CHX: chlorhexidine; ZUT: AgZ with KT-308 GIC; Zeomic: a synthetic AgZ; ASCOP: polyphenol-rich extract of *A. nodosum*

Table 2 IRR Values of Studies in the Systematic Review
Tablica 2. IRR vrijednosti istraživanja u sistematiziranom pregledu

	% User Agreement • % podudarnosti ocjenjivača	**Kappa**	**% data that are reliable (through Cohen's Kappa Test) • % pouzdanih podataka (Cohenov Kappa test)**	**Level of Agreement • Stupanj podudarnosti**
Sample Size • Veličina uzorka	80%	0.304	9.24%	Minimal • Minimalan
Control • Kontrola	97%	0.788	62.10%	Moderate • Umjeren
Blinding Operator • Zaslijepljeni istraživač	100.00%	1	100%	Almost Perfect • Gotovo savršen
Single Operator • Broj ocjenjivača	94%	0.693	40.80%	Moderate • Umjeren
Standardized Sample Prep • Priprema standardiziranog uzorka	74.30%	0.457	20.90%	Weak • Slab

as vaguely or insufficiently reporting the parameter. This was highlighted with the sample size parameter, in which the authors initially disagreed on whether the details surrounding the sample size were elaborated sufficiently. Another parameter with a low level of agreement was the standardized sample preparation. The disagreements among the authors regarding this parameter were explained by the variability in extent to which each article specifically stated that they conducted a standardized procedure. All disagreements were resolved after discussion among the authors.

Discussion

Thirty-five *in vitro* studies and randomized control trials were evaluated to assess the effects of zeolite on the antimicrobial and/or mechanical properties of dental materials. Generally, zeolite itself had little to no effect on antimicrobial properties unless there was an incorporation of ions such as silver or zinc. In addition, ion-incorporated zeolite exhibited prolonged ion release and can serve as a long-term antimicrobial material (4, 10-12). The present systematic review evaluates such properties by grouping the literature into four major categories based on the type of dental material tested: dental restorations, endodontics, prosthetics, and implants.

Dental Restorations

Regarding dental restorative materials, zeolite was generally combined with glass ionomer cements (GIC), resin cements, or bonding agents (3, 13-23).

Glass Ionomer Cement

When an ion-incorporated zeolite was combined with GIC, the antimicrobial effects were usually measured by an *in vitro* ion release profile or an agar diffusion test. As the ratio of AgZ by weight was increased, the inhibitory effect towards oral bacteria such as *S. mutans* would also increase (13). Similarly, 2% AgZ had the greatest antimicrobial properties against *S. milleri, S. aureus,* and *E. faecalis* compared to 0.2% and 0% AgZ (14). It is important to note that while GIC alone can only provide a rapid release of fluoride for two days, AgZ GIC can provide sustained release of silver ions for long periods of time (13). Similar antimicrobial results to AgZ can also be found in zinc-incorporated zeolite (ZnZ) against *E. coli, S. aureus, P. aureginosa, B. subtilis, and C. albicans* (15). In addition, zeolite in GIC can also have effective antimicrobial properties against *S. mutans* when it is loaded with chlorhexidine (16). For GIC used as root canal sealers, the antimicrobial effectiveness against *E. faecalis* had mixed results (17, 18). ZUT, a combination of 0.2% AgZ by weight (wt) and a GIC sealer, KT-308, inhibited *E. faecalis* growth significantly more than KT-308 alone, regardless of concentration and time (17). On the other hand, Padachey et al. and McDougall et al. both concluded that ZUT was not more effective than the other GIC (18, 19). The present results show that depending on the concentration of zeolite incorporated, GIC can have enhanced and sustained antimicrobial properties. However, the results may be affected by the use and type of GIC, and this could be a topic of further research.

smatrao da je parametar nejasno ili nedovoljno naveden. To je istaknuto kod parametra veličine uzorka u kojem se autori na početku nisu složili o tome jesu li detalji o veličini uzorka dovoljno razrađeni. Sljedeći parametar s niskom razinom slaganja bio je standardizirana priprema uzorka. Nesuglasice između autora u vezi s tim parametrom objašnjavaju se varijabilnošću u mjeri u kojoj je u svakomu radu posebno istaknuto da se provodio standardizirani postupak. Autori su sve nesuglasice riješili raspravom.

Rasprava

Ocijenjeno je trideset i pet randomiziranih kontroliranih istraživanja *in vitro* da bi se procijenili učinci zeolita na antimikrobna i/ili mehanička svojstva dentalnih materijala. Općenito, sam zeolit nije nimalo utjecao na antimikrobna svojstva, osim kada je bilo ugrađenih iona poput srebra ili cinka. Uz to, zeolit s ugrađenim ionima produljeno je oslobađao ione pa može poslužiti kao dugotrajni antimikrobni materijal (4, 10 – 12). Ovaj sistematizirani pregled ocjenjuje takva svojstva grupiranjem literature u četiri glavne kategorije na temelju vrste testiranoga dentalnog materijala. To su restaurativni materijali, endodoncija, proteze i implantati.

Restaurativni materijali

Kad je riječ o dentalnim restaurativnim materijalima, zeolit se obično kombinirao sa staklenoionomernim cementima (SIC), kompozitnim cementima ili adhezivima (3, 13 – 23).

Staklenoionomerni cement

Kada se zeolit s ugrađenim ionima kombinira sa SIC-om, antimikrobni učinci obično se mjere s pomoću *in vitro* profila oslobađanja iona ili agar-difuznim testom. Kako se povećava maseni udio AgZ-a, povećava se i inhibitorni učinak na oralne bakterije kao što je *S. mutans* (13). Slično tomu, 2 % AgZ-a imalo je najveća antimikrobna svojstva kad je riječ o *S. milleri, S. aureus* i *E. faecalis* u usporedbi s 0,2 % i 0 % AgZ-a (14). Važno je napomenuti da sam SIC samo dva dana može osigurati brzo oslobađanje fluora, a SIC s AgZ-om može osigurati kontinuirano oslobađanje iona srebra tijekom duljeg razdoblja (13). Sličan antimikrobni učinak kao AgZ ima i zeolit s ugrađenim cinkom (ZnZ) protiv *E. coli, S. aureus, P. aureginosa, B. subtilis* i *C. albicans* (15). Uz to, zeolit u SIC-u može učinkovito antimikrobno djelovati na *S. mutans* kada je napunjen klorheksidinom (16). Za SIC koji se upotrebljava kao sredstvo za brtvljenje korijenskih kanala rezultati antimikrobne učinkovitosti na *E. faecalis* bili su mješoviti (17, 18). ZUT, kombinacija 0,2 mas.% AgZ-a i SIC-a KT-308 inhibirala je rast *E. faecalis* znatno više od samoga KT-308, bez obzira na koncentraciju i vrijeme (17). S druge strane, Padachey i suradnici te McDougall i suradnici zaključili su da ZUT nije učinkovitiji od drugih SIC-ova (18, 19). Rezultati ovoga rada pokazuju da, ovisno o koncentraciji ugrađenoga zeolita, SIC može imati pojačana i dugotrajna antimikrobna svojstva. No uporaba i vrsta SIC-a mogu utjecati na rezultate, a to bi trebala biti tema daljnjih istraživanja.

Although the antimicrobial properties of GIC tended to have a direct relationship with the concentration of zeolite, the amount of zeolite that GIC can successfully uptake is limited by its resulting mechanical properties. The change in shear bond strength of zeolite-incorporated GIC depended on the type and use of the GIC (20, 21). ZUT presented higher shear bond strength than GIC Ketac-Endo alone and was not affected when it was conditioned by media such as calcium hydroxide, chlorhexidine, formocresol, and deionized water (20). However, adding zeolite to provisional cements may decrease the shear bond strength between the dentin and composite resin. Zeolite provisional cement was compared against bone hydroxyapatite provisional cement and showed an inferior bonding strength. A possible explanation for the decrease is that zeolite-incorporated provisional cement may contain more calcium hydroxide than the bone hydroxyapatite-incorporated cement (21). The compressive strength of zeolite-GIC also had varying results depending on the type and use of zeolite (13, 16). Lee et al. reported that although AgZ GIC showed higher compressive strength at 1% wt, it decreased when the concentration was higher than 3% (13). However, Kim et al. concluded that there was no significant difference in compressive or bond strength when small amounts of chlorhexidine-loaded zeolite nanoparticles (around 1% wt) were added to GIC (16).

Resin Cements

When zeolite was incorporated into resins, antimicrobial properties were improved against some microorganisms. Various ratios of AgZ and ZnZ inhibited *S. mutans* and *S. mitis* growth but did not inhibit *S. salivarius* or *S. sanguis* colonies. In contrast to what was observed with GIC, greater amounts of Ag-Zn-zeolite did not lead to greater amounts of antimicrobial activity in resins (3). After zeolite was modified with active diazonium, the compressive strength and flexural strength of the modified resin-based composite was either improved or remained the same (22). However, further research may be needed in this aspect of modifying zeolite because there is limited research on this topic.

Bonding Agents

Although zeolite alone did not improve the antimicrobial properties of bonding agents, the incorporation of AgZ did. Increasing the exchange time between AgZ and environmental ions can decrease biofilm formation of *S. mutans, S. gordonii,* and *S. sanguinis* on dental adhesives. Despite the linear relationship, increasing the amount of silver ions loaded into the zeolite so that the release time is greater than 40 minutes can result in damages to zeolite pore channels and uncontrollable silver ion release (23). Pretreating dentin with zinc zeolite may also enhance the shear bond strength between dentin and alloys using dental adhesives. This increase in shear bond strength was especially significant in the self-etch adhesive approach (24).

Endodontics

Zeolite in endodontics was generally added to calcium hydroxide and mineral trioxide aggregate (MTA) and used as root canal irrigants (25-31).

Iako su antimikrobna svojstva SIC-a bila u izravnom odnosu s koncentracijom zeolita, količina zeolita koju SIC može uspješno prihvatiti ograničena je mehaničkim svojstvima koja iz toga proizlaze. Promjena posmične čvrstoće veze SIC-a s ugrađenim zeolitom ovisila je o vrsti i upotrebi SIC-a (20, 21). ZUT je imao veću posmičnu čvrstoću od samoga SIC-a Ketac-Endo i nije bio pogođen medijima kao što su kalcijev hidroksid, klorheksidin, formokrezol i deionizirana voda (20). Međutim, dodavanje zeolita privremenim cementima može smanjiti posmičnu veznu čvrstoću između dentina i kompozitne smole. Privremeni cement sa zeolitom uspoređen je s privremenim cementom s koštanim hidroksiapatitom i imao je manju veznu čvrstoću. Moguće objašnjenje za smanjenje jest da privremeni cement s ugrađenim zeolitom može sadržavati više kalcijeva hidroksida od cementa s ugrađenim koštanim hidroksiapatitom (21). Za vlačnu čvrstoću SIC-a sa zeolitom također su dobiveni različiti rezultati, ovisno o vrsti i upotrebi zeolita (13, 16). Lee i suradnici izvijestili su da, iako je AgZ GIC imao veću tlačnu čvrstoću uz sadržaj od 1 %, ona se smanjila kada je koncentracija bila veća od 3 % (13). No Kim i suradnici zaključili su da nema značajne razlike u tlačnoj ili veznoj čvrstoći kada su u SIC dodane male količine nanočestica zeolita napunjenih klorheksidinom (oko 1 %) (16).

Kompozitni cementi

Kada se zeolit ugradi u smole, poboljšana su antimikrobna svojstva protiv nekih mikroorganizama. Razni omjeri AgZ-a i ZnZ-a inhibiraju rast *S. mutans* i *S. mitis*, ali nisu inhibirali kolonije *S. salivarius* ili *S. sanguis*. Za razliku od onoga što je zapaženo kod SIC-a, veće količine Ag-Zn-zeolita nisu rezultirale boljim antimikrobnim djelovanjem u smolama (3). Nakon što je zeolit modificiran aktivnim diazonijem, tlačna i savojna čvrstoća preinačenoga kompozita na bazi smole ili su poboljšane ili su ostale iste (22). No o tom aspektu modificiranja zeolita potrebna su daljnja istraživanja jer su dosadašnja o toj temi ograničena.

Adhezivi

Iako sam zeolit nije poboljšao antimikrobna svojstva adheziva, ugradnja AgZ-a jest. Povećanje vremena razmjene između AgZ-a i iona iz okoline može smanjiti stvaranje biofilma *S. mutans, S. gordonii* i *S. sanguinis* na dentalnim adhezivima. Unatoč linearnom odnosu, povećanje količine srebrovih iona u zeolitu tako da vrijeme oslobađanja traje dulje od 40 minuta može rezultirati oštećenjima kanala pora zeolita i nekontroliranim oslobađanjem srebrnih iona (23). Prethodna obrada dentina cinkovim zeolitom također može poboljšati posmičnu veznu čvrstoću između dentina i legura primjenom dentalnih adheziva. To povećanje posmične vezne čvrstoće bilo je posebno značajno kod samojetkajućih adheziva (24).

Endodoncija

Zeolit u endodonciji općenito se dodaje kalcijevu hidroksidu i mineralnom trioksidnom agregatu (MTA) te se upotrebljava kao irigans korijenskoga kanala (25 – 31).

Root Canal Irrigants

Although 2% AgZ did show statistically significant antimicrobial effectiveness as a root canal irrigant compared to the saline control, it did not exhibit as much effectiveness compared to common root canal irrigants such as 5% Sodium hypochlorite, 2% Chlorhexidine, and 0.10% Octenidine (OCT) (25). A possible reason why AgZ was not as effective as the other root canal irrigants against *E. faecalis, C. albicans*, and *S. aureus* growth is that it was not as effective at breaking down the biofilm of these microorganisms (25). When further studies on the mechanical properties of AgZ are published, a better conclusion can be drawn on whether it is worth using AgZ as a root canal irrigant.

Calcium hydroxide

Calcium hydroxide is considered an ideal intracanal medication in endodontics due to its unique ability to increase surrounding pH by dissociating in water to produce hydroxyl ions. Although the high pH denatures bacterial protein and breaks down cell walls, calcium hydroxide was not effective on all types of microorganisms that cause endodontic infections. Ghatole et al. showed that when AgZ was added to calcium hydroxide, antimicrobial property against *E. faecalis* is enhanced compared to the control or when chlorhexidine is added (26). Therefore, AgZ can potentially be added to intracanal medications, such as calcium hydroxide, to improve antimicrobial effectiveness.

MTA

When AgZ was added to MTA, it exhibited significant antimicrobial properties toward selected oral microflora. AgZ in MTA was effective against most oral microorganisms, such as *E. faecalis, S. aureus,* and *C. albicans*. However, it was not effective against *P. intermedia* and *A. israelii* (27-28). No big differences were found in the types of microbes inhibited by 0.2% and 2% AgZ MTA, but 2% AgZ MTA demonstrated significantly higher inhibitory effects than 0.2% AgZ MTA throughout a 72-hour period. Specifically, 2% AgZ demonstrated the highest amount of silver ion release at 24 hours (27). In addition, 2% AgZ was found to have greater antimicrobial properties compared to MTA with 2% chlorhexidine (28). Therefore, 2% AgZ could serve as a potential additive in MTA to enhance its antimicrobial properties.

Although zeolite significantly increased the antimicrobial properties of MTA, it did negatively affect physical properties such as setting time, water absorption, push-out bond strength and compressive strength (29-31). Setting time decreased as the ratio of 2% AgZ increased, and water absorption was the lowest when 2% AgZ was incorporated into MTA compared to the MTA-only control (29). In addition, adding Ag-Zn-Ze composite had a negative effect on the push-out bond strength and compressive strength of MTA (30-31). A possible reason for the decrease in push-out bond strength is that zeolite is very porous in its structure. When water molecules reside in the pores, they can disturb the hydration and crystallization processes of MTA (30). In conclusion, although zeolite may enhance the antimicrobial proper-

Iriganski korijenskih kanala

Iako je 2 % AgZ-a imalo statistički značajnu antimikrobnu učinkovitost kao sredstvo za ispiranje korijenskih kanala u odnosu prema fiziološkoj otopini, nije pokazao toliku učinkovitost u usporedbi s uobičajenim sredstvima za ispiranje kanala kao što su 5-postotni natrijev hipoklorit, 2-postotni klorheksidin i 0,10-postotni oktenidin (OKT) (25). Mogući razlog zašto AgZ nije bio toliko učinkovit kao druga sredstva za ispiranje korijenskoga kanala kad je riječ o rastu *E. faecalis, C. albicans* i *S. aureus* jest taj što nije bio toliko učinkovit u razgradnji biofilma tih mikroorganizama (25). Kada se objave daljnja istraživanja o mehaničkim svojstvima AgZ-a, moći se dati bolji zaključak o tome treba li upotrebljavati AgZ kao sredstvo za ispiranje korijenskog kanala.

Kalcijev hidroksid

Kalcijev hidroksid smatra se idealnim intrakanalnim lijekom u endodonciji zbog svojega jedinstvenog svojstva da poveća okolni pH razdvajanjem u vodi stvarajući hidroksilne ione. Iako visoki pH denaturira bakterijski protein i razbija stanične stijenke, kalcijev hidroksid nije učinkovito djelovao na sve vrste mikroorganizama koji uzrokuju endodontske infekcije. Ghatole i suradnici pokazali su da se dodavanjem AgZ-a kalcijevu hidroksidu pojačavaju antimikrobna svojstva protiv *E. faecalis* u usporedbi s kontrolom ili dodavanjem klorheksidina [26]. Zato se AgZ može dodati intrakanalnim lijekovima, kao što je kalcijev hidroksid, radi poboljšanja antimikrobne učinkovitosti.

MTA

Kad je AgZ dodan MTA-i, imao je izražena antimikrobna svojstva prema odabranim oralnim mikrobima. AgZ u MTA-i učinkovito je djelovao na većinu oralnih mikroorganizama, kao što su E. *faecalis, S. aureus* i *C. albicans*. No nije bio učinkovit kad je riječ o *P. intermedia* i *A. israelii* [27 – 28]. Nisu pronađene velike razlike u vrstama mikroba koje su inhibirali 0,2 % i 2 % AgZ MTA-e, ali 2 % AgZ MTA-e imao je značajno veći inhibitorni učinak od 0,2 % AgZ MTA-e tijekom razdoblja od 72 sata. Točnije, 2 % AgZ-a pokazalo je najveću količinu oslobađanja iona srebra u 24 sata (27). Uz to, utvrđeno je da 2 % AgZ-a ima bolja antimikrobna svojstva u usporedbi s MTA-om s 2 % klorheksidina (28). Zato bi 2 % AgZ-a moglo poslužiti kao aditiv u MTA-i za poboljšanje njezinih antimikrobnih svojstava.

Iako je zeolit značajno povećao antimikrobna svojstva MTA-e, negativno je utjecao na fizikalna svojstva kao što su vrijeme stvrdnjavanja, apsorpcija vode, vlačna i tlačna vezna čvrstoća (29 – 31). Vrijeme stvrdnjavanja smanjivalo se kako se povećavao omjer 2 % AgZ-a, a apsorpcija vode bila je najmanja kada je 2 % AgZ-a ugrađeno u MTA-u u usporedbi s kontrolom gdje je bila samo MTA (29). Uz to, dodavanje kompozita Ag-Zn-Ze negativno je utjecalo na vlačnu i tlačnu veznu čvrstoću MTA-e (30 – 31). Mogući razlog za smanjenje vezne čvrstoće jest taj što je struktura zeolita vrlo porozna. Kad se molekule vode nalaze u porama, mogu poremetiti procese hidratacije i kristalizacije MTA-e [30]. Zaključno, iako zeolit može pojačati antimikrobna svojstva MTA-e, on smanjuje mehanička svojstva. Zato su potrebna daljnja istraties of MTA, it does reduce the mechanical properties. Thus, further research is needed to determine the proper concentration of zeolite that may be incorporated into MTA, if any, to improve its antimicrobial properties without compromising its mechanical properties.

Prosthesis

Zeolite in prosthesis was added to both acrylic resin and non-acrylic materials, such as ceramic (32-38).

Non-Acrylic Resins

The non-acrylic materials that were tested with zeolite ranged from soft prosthetic liners to all-ceramic prosthesis. Adding AgZ to soft liners improved its antimicrobial properties against *C. albicans* and gram-negative bacteria while also retaining its viscoelastic properties (32). Regarding the mechanical properties, the applications of zeolite into ceramic prosthesis generally focused on sodalite zeolite (33-36), a subtype of zeolite that can easily infiltrate other material due to its selectivity and strong catalytic activity (33). In alumina and zirconium toughened alumina (ZTA) ceramic prostheses, sodalite zeolite-infiltrated samples had higher bond strength than the commercial glass-infiltrated samples between ceramic core and porcelain (34). In addition, all sodalite zeolite-infiltrated samples showed flexural strength above the acceptable ranges considered by the ISO (35-36). Furthermore, some studies have shown that the zeolite-infiltrated samples had a significantly higher flexural strength and hardness in comparison with glass-infiltrated control, especially when heated to 1600°C (35). Finally, sodalite zeolite-infiltrated ZTA has one of the highest fracture toughness and elastic modulus values compared to its glass-infiltrated counterparts (33). Therefore, sodalite zeolite infiltrated samples can serve as a potential alternative to the glass infiltrated ZTA due to superior properties in bond strength, flexural strength, Vickers hardness, fracture toughness, and elastic modulus (33-36).

Acrylic Resin

AgZ increased the antimicrobial properties of acrylic resin against oral microbes such as *S. mutans, F. nucleatum,* and *C. albicans*. Self-cured acrylic resins tend to absorb copious amounts of water and do not easily polymerize, resulting in the accumulation of periodontal disease-causing bacteria. AgZ-incorporated acrylic resin may potentially resolve this issue since it effectively diminished the attachment of *S. mutans, F. nucleatum, and C. albicans* to polymethylmethacrylate (PMMA) and lasted for up to 45-60 days (37-39). Similarly, 2.5% Ag-Zn-Ze was effective at inhibiting *C. albicans* and *S. mutans* when added to PMMA (40). Therefore, both AgZ and Ag-Zn-Ze may be potentially viable options to improve the antimicrobial properties of PMMA.

However, depending on the percentage added, AgZ may negatively affect the mechanical properties of acrylic resin (38-41). Adding AgZ with concentrations of 2.5% and higher, depending on the type of acrylic resin, will significantly reduce the impact and flexural strength (38, 40-41). However, some types of heat-cured acrylic resin, such as QC20 and Lucitone 550, may still satisfy the standard for denture

živanja kako bi se utvrdila odgovarajuća koncentracija zeolita koji se može ugraditi u MTA-u, ako postoji, kako bi se poboljšala njegova antimikrobna svojstva, a da se pritom ne naruše ona mehanička.

Protetika

Zeolit u protezi dodaje se akrilatnoj smoli i neakrilatnim materijalima poput keramike (32 – 38).

Neakrilatne smole

Neakrilatni materijali koji su ispitivani sa zeolitom kretali su se od materijala za mekano podlaganje proteza do potpuno keramičkih proteza. Dodavanjem AgZ-a materijalima za mekano podlaganje poboljšala su se njegova antimikrobna svojstva protiv *C. albicans* i gram-negativnih bakterija, a istodobno su se zadržala viskoelastična svojstva (32). Kad je riječ o mehaničkim svojstvima, primjena zeolita u keramičkim protezama uglavnom se fokusirala na sodalitni zeolit (33 – 36), podvrstu zeolita koja se lako može infiltrirati u drugi materijal zbog selektivnosti i jake katalitičke aktivnosti (33). U keramičkim protezama od ojačane glinice i cirkonijeva oksida (ZTA), uzorci infiltrirani u zeolit sodalitom imali su veću veznu čvrstoću od komercijalnih uzoraka infiltriranih staklom između keramičke jezgre i obložne keramike (34). Uz to, svi uzorci infiltrirani zeolit sodalitom imali su savojnu čvrstoću iznad prihvatljivih granica prema ISO standardu (35 – 36). Nadalje, u nekim istraživanjima autori su pokazali da su uzorci infiltrirani zeolitom imali znatno veću savojnu čvrstoću i tvrdoću u usporedbi s kontrolom infiltriranom staklom, posebno kada su zagrijani na 1600 °C (35). Konačno, ZTA sa zeolit sodalitom ima jednu od najvećih vrijednosti žilavosti i modula elastičnosti u usporedbi s materijalima infiltriranima staklom (33). Zato uzorci infiltrirani zeolit sodalitom mogu poslužiti kao potencijalna alternativa staklom infiltriranom ZTA-u zbog superiornih svojstava kad je riječ o veznoj i savojnoj čvrstoći, tvrdoći prema Vickersu, žilavosti i modulu elastičnosti (33 – 36).

Akrilatne smole

AgZ je povećao antimikrobna svojstva akrilatnih smola kad je riječ o oralnim mikrobima kao što su *S. mutans, F. nucleatum* i *C. albicans*. Autopolimerizirajuće akrilatne smole imaju tendenciju upijanja obilnih količina vode i ne mogu se lako polimerizirati, što rezultira nakupljanjem parodontopatogenih bakterija. Akrilatna smola ugrađena u AgZ može riješiti taj problem jer učinkovito smanjuje vezanje *S. mutans, F. nucleatum* i *C. albicans* za polimetilmetakrilat (PMMA) u trajanju od 45 do 60 dana (37 – 39). Slično tomu, 2,5 % Ag-Zn-Ze-a bilo je učinkovito u inhibiciji *C. albicans* i *S. mutans* kada se doda u PMMA (40). Zato i AgZ i Ag-Zn-Ze mogu biti dobre opcije za poboljšanje antimikrobnih svojstava PMMA-e.

No ovisno o dodanom postotku, AgZ može negativno utjecati na mehanička svojstva akrilatne smole [38 – 41]. Dodavanje AgZ-a u koncentracijama od 2,5 % i više, ovisno o vrsti akrilatne smole, značajno će smanjiti savojnu čvrstoću (38, 40 – 41). No neke vrste toplinski polimeriziranih akrilatnih smola, poput QC20 i Lucitone 550, još uvijek mogu zadovoljiti standard za akrilatne proteze koji zahtijeva savojacrylics, which requires flexural strength to be higher than 65 MPa (38, 40). Depending on the concentration of zeolite added, both mean tensile strength and bending strength decreased. It was recommended to add less than 4% zeolite wt to keep adequate mechanical strength, and 2% when factoring in both mechanical and fungicidal effects (39). Therefore, low percentages of silver-zinc antimicrobial zeolites added to polymethylmethacrylate can be a valuable alternative for antimicrobial effects, which could help prevent common oral infections such as denture stomatitis (38).

Implants

Numerous applications of zeolite also extend to antibacterial coatings on implants. Although there is not a great amount of literature on this topic, coating titanium implants with AgZ was effective in inhibiting methicillin-resistant *S. aureus* (MRSA) growth (42). This positive outcome, combined with zeolite's superior biocompatibility, may render zeolite a possible new material to be used in orthopedic implants.

Limitations of the study

Since most of the literature covered in the present review consisted of *in vitro* studies, it is important to note that there is a lack of widely accepted and clear criteria for assessing the risk of bias and quality of *in vitro* studies. To address this problem, a risk of bias test used in a previous study was adapted and used in this review (7). In the future, there should be more *in vivo* studies performed in order to better understand the effects of zeolite on the oral environment.

Conclusion

The available evidence collected through the present systematic review showed that ion-incorporated zeolite demonstrated enhanced antimicrobial properties when incorporated into dental materials. When ion-zeolite was incorporated into non-acrylic prosthetic materials, the mechanical as well as the antimicrobial properties were enhanced. GIC demonstrated the greatest antimicrobial effectiveness with 2% zeolite wt while maintaining mechanical properties between 1-3% zeolite wt. Therefore, it was recommended to use a concentration of 2% zeolite wt with GIC to optimize both factors. Lower concentrations such as 0.2-2% wt were recommended for MTA and acrylic prosthetic materials, which showed the greatest decrease in mechanical properties when combined with zeolite.

Conflict of interest

The authors report no conflict of interest.

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nu čvrstoću veću od 65 MPa (38, 40). Ovisno o koncentraciji dodanoga zeolita, smanjile su se i srednja vlačna čvrstoća i savojna čvrstoća. Preporučeno je dodavanje manje od 4 % zeolita kako bi se zadržala odgovarajuća mehanička svojstva, a 2 % kada se uzimaju u obzir i mehanički i fungicidni učinak (39). Zato nizak postotak antimikrobnog srebrno-cinkova eolita dodanoga polimetilmetakrilatu može biti vrijedna alternativa za postizanje antimikrobnog učinka, što bi moglo pomoći u prevenciji uobičajenih oralnih infekcija poput protetičkog stomatitisa (38).

Implantati

Brojne primjene zeolita također se protežu na antibakterijske obloge na implantatima. Iako o toj temi nema mnogo radova, oblaganje titanijskih implantata AgZ-om učinkovito je inhibiralo rast bakterije *S. aureus* otporne na meticilin (MRSA) (42). Taj pozitivni ishod, u kombinaciji s vrhunskom biokompatibilnošću, zeolit može učiniti mogućim novim materijalom koji će se upotrebljavati u ortopedskim implantatima.

Ograničenja istraživanja

Budući da su većina radova obrađenih u ovom pregledu istraživanja *in vitro*, važno je napomenuti da nedostaju široko prihvaćeni i jasni kriteriji za procjenu rizika od pristranosti i kvalitete istraživanja *in vitro*. Kako bi se riješio taj problem, u ovom je pregledu prilagođen i korišten test rizika od pristranosti iz prethodnoga istraživanja (7). U budućnosti bi trebalo provesti više istraživanja *in vivo* da bi se bolje shvatili učinci zeolita u intraoralnom okružju.

Zaključak

Dokazi prikupljeni u ovomu sistematiziranom pregledu pokazali su da zeolit s ugrađenim ionima ima pojačana antimikrobna svojstva kada se uključuje u dentalne materijale. Kada se zeolit s ugrađenim ionima inkorporira u protetičke materijale koji nisu na bazi akrilata, poboljšana su mehanička i antimikrobna svojstva. SIC je imao najveću antimikrobnu učinkovitost s 2 % masenoga udjela zeolita, zadržavajući mehanička svojstva između 1 i 3 % udjela zeolita. Zato je preporučena koncentracija od 2 % zeolita u SIC-u za optimizaciju obaju čimbenika. Niže koncentracije poput 0,2 do 2 % preporučene su za MTA i akrilatne protetičke materijale koji su pokazali najveće narušavanje mehaničkih svojstava u kombinaciji sa zeolitom.

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Autori ne navode sukob interesa.

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Doprinos autora: **J.H.** - prikupljanje, organiziranje i provjeravanje podataka, softverske aplikacije za analizu podataka, priprema i pisanje izvornog članka; **S.L.** - planiranje, organiziranje i provjeravanje podataka, pomoć u dizajniranju softvera, priprema i pisanje izvornog članka; **F.M.** - Statistički izračuni, analiza i interpretacija podataka, pregled i uređivanje članka; **K.P.** - savjetovanje, pregled i uređivanje članka; **F.O.** - Dizajn i nadzor studijskog projekta, prikupljanje financijskih sredstava, kritična revizija članka, konačno odobrenje verzije koja će se objaviti.

Sažetak

Svrha istraživanja: Zeolit s ugrađenim ionima često je korišten antimikrobni materijal koji se proučava za različite primjene u stomatologiji. Trenutačno ne postoji ni jedan drugi sistematizirani pregledni rad u kojemu bi se ocjenjivala učinkovitost zeolita u svim dentalnim materijalima. Svrha ovoga istraživanja bila je pregledati svu objavljenu literaturu u kojoj su analizirani antimikrobni učinci i/ili mehanička svojstva zeolita kao restaurativnog materijala u stomatologiji. **Materijal i metode:** Slijedeći smjernice PRISMA-e, od 1. lipnja do 17. kolovoza 2020. provedeno je iscrpno pretraživanje baza Pubmed, Ovid Medline, Scopus, Embasa te Dentistry i Oral Sciences Source. Nisu korištena jezična ili vremenska ograničenja. Odabrani su samo cjeloviti članci kojima je tema bila upotreba zeolita u dentalnim materijalima, uključujući kompozitne materijale, adhezive, cemente, restaurativne intrakorijenske materijale, podloge te materijale u protetici, implantologiji i endodonciji. **Rezultati:** Na početku su pronađena 1534 istraživanja, od kojih je isključeno 687 duplih zapisa. Nakon pregleda naslova, sažetka i cjelovitih tekstova, ostalo je 35 radova koji su uključeni u kvalitativnu sintezu. Za svaki od njih proveden je test pouzdanosti među ocjenjivačima (IRR) koji je obuhvaćao postotak slaganja i postotak pouzdanosti. **Zaključak:** Iako zeolit s ugrađenim ionima može pojačati antimikrobna svojstva dentalnih materijala, mehanička svojstva nekih mogu biti ugrožena, poput MTA i akrilatne smole. Stoga, s obzirom na to da pogoršanje mehaničkih svojstava ovisi o koncentraciji zeolita u restaurativnom materijalu, općenito se preporučuje dodavanje 0,2 do 2 mas.% zeolita.

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