

PULPAL BIOCOMPATIBILITY AND SOLUBILITY OF CONTEMPORARY LUTING CEMENTS IN FIXED PROSTHODONTICS: A SYSTEMATIC REVIEW

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Received: 12 April 2025; Revised: 29 July 2025; Accepted: 03 August 2025

<https://doi.org/10.51847/Kyyq3Lycjo>

ABSTRACT

The objective of this systematic review was to assess, evaluate, and analyze the pulpal biocompatibility and solubility of various contemporary luting cements utilized in fixed prosthodontics. The scope of the evaluation included emphatically self-adhesive resin cement and resin-modified glass ionomer cements, which are some of the most used cements in restorative practices in Saudi Arabia and other countries around the globe. Electronic searches were performed in PubMed, Scopus, ScienceDirect, and Google Scholar until April 2024. Selected studies evaluated pulpal responses for biocompatibility or the solubility properties of permanent luting cements incisively and in vitro or in vivo. Studies were screened with PRISMA guidelines, and the risk of bias was assessed employing conventional methods. Ten studies matched the eligibility criteria. Significant results were obtained from resin-based luting cements like Panavia F, Multilink Automix, and Variolink II, which demonstrated lesser water sorption and solubility values in comparison to Fuji Plus, a glass ionomer resin modified cement. All materials were found to be more soluble in acidic environments, although more stable in resin cements. Biocompatibility testing conducted through cytokine release and MTT assays indicated that the majority of resin cements caused minimal inflammatory response and were deemed non-toxic. There is also some potential for pulpal irritation associated with increased cytokine release with some of the resin-modified cements. These results corroborate the rationale for preferring resin-based luting materials in the clinical setting of Saudi Arabia, where dental professionals need dependable and enduring cementation options. Additional region-targeted studies and in vivo research are warranted.

Key words: Luting cements, Biocompatibility, Crowns, Fixed prosthesis.

Introduction

Restorative dentistry practices depend largely on luting processes to protect indirect restorations. There are now many options available in the form of luting cement and prosthetic substrates, each having its biological, physicochemical, and esthetic merits [1]. It is arguable whether luting cement stays as a temporary substance or is permanent. The former splits into two unique subsets, provisional luting cements, which are more commonly referred to as temporary cement. Among this group, the most common is calcium hydroxide cement and zinc oxide cement. Any material that binds to dental and/or prosthetic substrates is classified as permanent luting cement [2-4]. Materials like zinc phosphate and silicate cement are considered weak luting, while materials like polycarboxylate cement and glass ionomer are medium strength. The present study focused exclusively on a high strength that may be cured by chemical/self-activation, light curing, or a combination [5-7]. In terms of bonding, high strength, however, is graded into subclasses of luting resin cement and self-adhesive resin cement. Traditionally, surface bonding for luting resin cement has needed extensive surface preparation for attachment.

The best method for achieving direct bonding to surfaces is through the application of self-adhesive resin cement, which contains silanes and very high-functional monomers like 10-MDP that ensure bonding. These were the first to surpass the rest of the resin cements in popularity because of their construction and potential therapeutic uses [8, 9]. However, using such materials means that pretreatment processes like acid etching do not need to be done, although general practitioners still need guidance on bond application directives [6, 7, 10, 11]. The long-term clinical outcomes of the permanent luting cement, particularly those reinforced with resin, such as resin-modified glass ionomer cement and resin-based cement, need to be emphasized. The low solubility of the cement could potentially mitigate damage to the pulp and secondary caries due to the low damage of cement dissolution [12, 13]. The application of such materials for casting posts and core build-ups is likely to reduce the risk of root fractures. Moreover, indirect aesthetic ceramic and composite restorations are reported to have enhanced durability and fracture resistance when done with adhesive resin-based cements [14-16].

It is also accepted that certain preparations, also known as predispositional treatments, must be accomplished to achieve a perfect bond between the tooth and the prosthetic

surfaces. As much as the training and the skill of the operator, the quality of particular tools at hand and their clever execution of surface pretreatments are crucial to achieving successful outcomes. In the past decade, a new class of resin cements with specific properties has emerged very rapidly. It might soon allow practitioners to provide adequate bond strength without complex and user-friendly surface treatments. However, self-sticking resin cements still require more research to compete with conventional or self-adhesive resin-based and resin-modified glass ionomer cements (RMGICs) [17-19].

Materials and Methods

This systematic review was conducted according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. An exhaustive search of the literature was conducted in four electronic databases: PubMed, Scopus, ScienceDirect, and Google Scholar. The search was restricted to articles published prior to April 2024 and utilized terms including "luting cement," "resin cement," "biocompatibility," "solubility," "water sorption," and fixed prosthodontics."

Inclusion criteria

- Studies, both in vitro and in vivo, are looking at pulpal biocompatibility, luting cement biocompatibility, and solubility.
 - Research investigating high-strength luting cements like resin-modified glass ionomer, self-adhesive resin cements, and dual-cure resin cements.
 - Articles published in the English language.
 - Studies in the field of fixed prosthodontics.

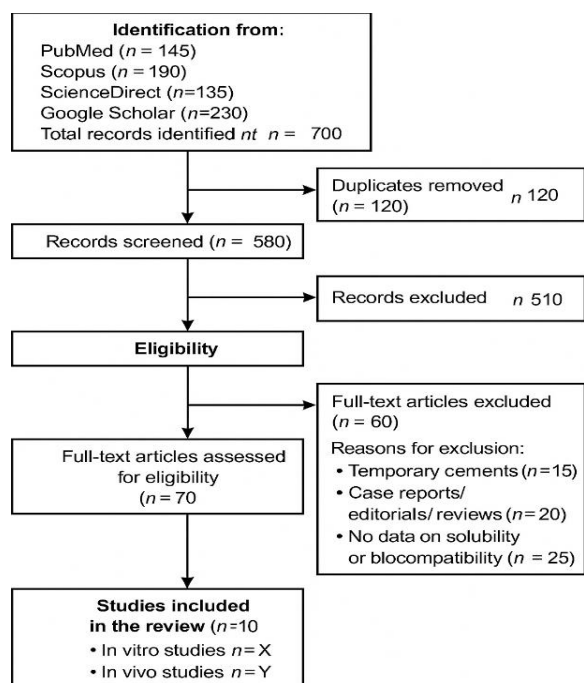


Figure 1. PRISMA flow chart diagram

Exclusion criteria

- Studies that only focused on the use of temporary cements.
- Case reports, editorials, and literature reviews.
- Research that does not evaluate solubility or pulpal response outcomes.

Data extraction

Two independent reviewers screened and reported data on the methodologies, designs, sample/patient count, employed materials, and key findings of the Studies. All disputes were settled through consensus or by a third-party adjudicator (Figure 1).

Quality assessment

The diverse studies were evaluated using tailored in vitro and in vivo standard quality assessment tools designed for experimental research. Based on the study's design, sampling control, blinding, and statistical analysis, the risk of bias was evaluated as low, moderate, or high.

Results and Discussion

The work of Gerdolle *et al.* (2008) [20] was focused on assessing the water sorption and solubility characteristics of a polyacid-modified composite resin and two composite resins, Variolink II and Panavia F, in relation to a resin modified glass ionomer cement, Fuji Plus, and also has the dual aim of quantifying the water absorption and determining the solubility characteristics of five constructed composite disks of each type of cement. The study followed the pattern of preparing five disk specimens (each 15mm in diameter and 1mm thick) per material, which also had to go through a period of desiccation. Distilled water was then added, and the specimens were left to sit for a week. After this time, the specimens were weighed daily for 35 days alongside the measurements of desiccation. The water solubility levels and rates were measured based on the mass changes throughout the process, considering the ISO 4049 rules. Out of all the materials used in the study, Fuji Plus was determined to possess the highest value of water solubility and absorption. Further into the study, it was found that higher water solubility and absorption levels were noted for the composite resin-based cements compared to the Resinomer counterpart.

In contrast, low levels were observed for both Variolink II and Panavia F. The study concluded that those composite resin luting cements, which are based on substrate-adapted materials for long-term clinical use, have lower water absorption and solubility variables. In contrast, the Fuji Plus reinforced glass version became the cement that gets modified by the glass and does not withstand sustained humid environments. More extensive examination is needed regarding the enduring clinical use of these materials, particularly concerning the changes in the oral environment.

The purpose of the study by Yoshida *et al.* (1998) [21] was to evaluate the solubility of three types of resin cements: All-Bond C&B, Panavia 21, and Super-Bond C&B, and compare them with three conventional luting cements (Zinc Phosphate, Polycarboxylate, and Glass-Ionomer Cements) in varying media. Specimens were prepared and submerged in two types of media: distilled water and a pH 4.0 lactic acid solution, for 30 days. Solubility was evaluated by measuring weight as a function of time, following a modified version of the ADA specification test. In both media, resin cements showed significantly lower solubility compared to conventional luting cements. All cements demonstrated an increase in solubility in the acidic solution, but the traditional cements were affected to a greater extent. The resin luting cements' stronger resistance to solubility, especially in acidic conditions, makes them more favorable when long-term presence in the oral cavity is required. Further research should focus on the potential usefulness of these results clinically, especially for patients with an acidic oral environment.

The research performed by Gavranović-Glamoč *et al.* (2020) [22-24] aimed to Evaluate and compare the solubility of luting cements comprising of resin modified glass ionomer cement (GC Fuji Plus) and two resin cements (Multilink Automix and Variolink II) in distilled water and artificial saliva with different pH (7.4 and 3.0). A total of 45 specimens (15 for each cement) were prepared according to ISO 4049:2009 standards. The measurement of solubility was conducted based on the weight changes of the specimens pre- and post-immersion and desiccation. Mann-Whitney U Test with a post hoc comparison was conducted for evaluative statistical analysis. GC Fuji Plus showed significantly higher solubility compared to the resin cements in all solutions. Multilink Automix showed greater solubility than Variolink II in acidic artificial saliva with a pH of 3.0. The solution's pH greatly impacted the solubility of GC Fuji Plus, while the other resin cements were unaffected. The composition of the luting cements and the pH of the environment dictate how the substance is eroded. The resin cements were more stable than the resin-modified glass ionomer cements across the varied pH levels. It is recommended that the impacts of changing pH over long durations be investigated on the solubility and performance of different luting cements in the oral cavity.

Kwon *et al.* (2015) [25] examined the biocompatibility of different dental luting cements by measuring the release of the pro-inflammatory cytokines IL-1 α and IL-8, using a human oral fibroblasts and keratinocytes culture assay [26, 27]. Immortalized human gingival fibroblasts and oral keratinocytes received different luting cement extracts for varying time frames. From the supernatants, cytokine concentrations were quantified and juxtaposed against traditional MTT viability assay results. Traditional MTT assays suggested that only one sample was cytotoxic with extended exposure, and the rest were biocompatible. However, the more complex picture provided by cytokine

measurements showed that many factors, such as the type of cell, the cytokine in question, and the duration of exposure, affected outcomes. Measurement of pro-inflammatory cytokines yields a more comprehensive assessment of biocompatibility, which in this case reveals the considerable importance of using inflammatory response assays alongside viability assays. More refined estimates of clinical-materials compatibility could be made by integrating inverse cytokine profiling aimed at estimating material-induced inflammation trajectories.

This study, by Jamel *et al.* (2020) [28], aimed to evaluate the water absorbance and solubility of different dental cements at different time points to assess their behavior in the oral cavity [29]. Different samples of dental cements were prepared and submerged in distilled water. Water sorption and solubility measurements were conducted at certain intervals to assess changes over time. The research found that resin-based cements had lower water sorption and solubility compared to glass ionomer resin cements and compomers. All materials changed over time, but the resin-based cements were relatively more stable. Over time, resin-based cements demonstrated better resistance to water sorption and solubility, indicating their potential clinical applicability for sustained use. These materials need to be evaluated in clinically realistic scenarios, with an emphasis on the polyaxial interactions of the oral cavity for extended durations.

Radhakrishnan *et al.* (2023) [30] completed a study assessing and comparing the sorption and solubility of a glass ionomer cement (GIC), a resin-modified glass ionomer cement (RMGIC), and a resin cement luting cement in distilled water, artificial saliva, and carbonated water [31]. A total of 126 disc-shaped specimens (10 mm diameter x 2 mm height) were fabricated, with 42 specimens for each type of cement. Fourteen specimens of each material were immersed in 20 ml of each medium. After 37°C incubation, mass and dimensions were taken at multiple intervals over five weeks. Subsequently, the specimens were desiccated for five weeks. Water sorption and solubility were calculated based on weight changes. Across all media tested, the resin cement showed the least amount of sorption and solubility. RMGIC showed the highest solubility in distilled water, while GIC showed the highest solubility in artificial saliva and carbonated water. The pH of the storage media greatly impacted the values of sorption and solubility, with more acidic environments enhancing the values. The study assessed that resin cement is more stable and less prone to degradation in various oral environments compared to GIC and RMGIC. The estimated lifespan of dental restorations is critical for selecting luting cement, and it is directly linked to the particular oral environment. The clinical implications for predicting the performance of luting cements should be adjusted to include longer waiting times and more complex dynamic simulations of oral environments, which would include the presence of enzymes and changing pH levels.

The objective of the study conducted by Leal *et al.* (2016) [32] was to assess the water sorption and solubility of different luting agents beneath ceramic laminates of varying translucency [33]. In accordance with ISO 4049 standards, the study prepared specimens of various luting agents and conducted water sorption and solubility tests. The study explored the effects of ceramic laminate translucency on these properties. It was concluded that the degree of translucency of ceramic laminates did influence the water sorption and solubility of the luting agents located underneath. Among the four types of cements tested, resin-based cements had the lowest water sorption and water-soluble materials. The water-related properties of luting agents can be affected by the degree of translucency of the overlying ceramic laminates. Moreover, resin-based cements were found to be more stable and less susceptible to degradation in these conditions. These results raise important questions about the restoration's long-term endurance framed by various ceramic translucent layers, which should be investigated in future studies.

Bharali *et al.* (2017) [34] conducted the research intending to assess the sorption and solubility of four different luting cements after immersion in artificial saliva with varying levels of pH. For this purpose, specimens of four luting cements were fabricated and placed in artificial saliva solutions with a pH of 5 and 7. The measurements of sorption and solubility were carried out according to ISO measures. It was found during the study that the pH of the artificial saliva plays a significant role in the sorption and solubility of luting cements. The resin-based cements had lower values than the glass ionomer cements, particularly in the acidic conditions. These findings suggest that resin-based luting cements are less susceptible to degradation in low pH situations, which is advantageous for patients with acidic oral environments. As with all in vitro studies, these findings should be evaluated alongside long-term clinical studies to test the broad range of conditions these cements might experience in everyday use.

In the study performed by Ülker *et al.* (2013) [35], "To assess the cytotoxic effects of temporary luting cements using two-dimensional and three-dimensional cultures of

bovine dental pulp-derived cells," they sought to evaluate the effects of temporary luting cements on dental pulp cells. It involved using bovine dental pulp-derived cells grown in two-dimensional and three-dimensional cultures. The two-dimensional cultures were subjected to several different extracts of the temporary luting cement. Additionally, cytotoxicity was evaluated using cell viability assays. The findings suggested that the tested cements exhibited varying levels of necrosis. Several cements were found to have more toxic effects, especially in the three-dimensional culture models, which simulate more in vivo environments. Temporary luting cements can pose cytotoxic effects on dental pulp cells, the level of which is dependent on the composition of the cement. Focus should be placed on the formulation of a temporary luting cement that incorporates reduced cytotoxicity for better pulpal health during provisional restorations.

Shams *et al.* (2024) [36] conducted this particular study to assess the mechanical properties, particularly the shear bond strength and flexural strength, of a new dual-cure, universal bioactive luting cement (BioCem®) in comparison to a conventional glass ionomer cement (Fuji I®). Sixty extracted deciduous molars underwent random division into two equal groups, one of which was cemented using Fuji I®, while the other was cemented using BioCem®. The measurement of bond strength was carried out using a universal testing machine, whereas the assessment of flexural strength was conducted utilizing standardized test specimens.

In comparison to Fuji I®, BioCem® exhibited greater flexural strength but lower shear bond strength. This means that while BioCem® can withstand mechanical stress, it does not have GIC-like bonds to depend on. Although BioCem® demonstrates potential for use as a luting agent due to its high flexural strength, the low shear bond strength indicates that further improvements are needed to the formulation to augment adhesion. Additional work is needed to improve the adhesive properties of BioCem® and assess its clinical effectiveness over extended periods for different restorative procedures. All of the studies are summarized in **Table 1**, given below.

Table 1. Summary of included studies

Author (Year)	Study Purpose	Methodology	Samples / Patients	Materials Used	Results
Gerdolle <i>et al.</i> (2008) [20]	To test the water sorption and solubility of four luting cements.	ISO-based desiccation, water immersion, and reweighing.	5 discs of each material.	Variolink II, Panavia F, Resinomer, Fuji Plus.	Fuji Plus had the highest values. Resinomer is also high. Variolink II and Panavia F had low and stable values.

Yoshida <i>et al.</i> (1998) [21]	To compare the solubility of resin vs. conventional cements in water and acid.	Measured weight loss over 30 days in water and pH 4.0 lactic acid.	Multiple specimens per cement.	All-Bond C&B, Panavia 21, Super-Bond C&B, zinc phosphate, polycarboxylate, glass-ionomer.	Resin cements had lower solubility, even in acid. Conventional ones degraded more.
Gavranović-Glamoč <i>et al.</i> (2020) [22]	To compare the solubility of luting cements in different pH environments.	Followed ISO 4049; weighed before and after immersion/desiccation.	45 total (15 per cement).	GC Fuji Plus, Multilink Automix, Variolink II.	GC Fuji Plus dissolved the most. Resin cements were more stable. Acidic pH affected Fuji Plus more.
Kwon <i>et al.</i> (2015) [25]	To assess biocompatibility using cytokine release from human cells.	Cells exposed to cement extracts; cytokines (IL-1 α , IL-8) measured.	Human gingival fibroblasts & keratinocytes.	Various luting cements (not all named).	Only one cement was cytotoxic by MTT. Cytokines showed more complex inflammation reactions.
Jamel (2020) [28]	To study water sorption and solubility over time.	Immersion in distilled water and periodic measurement.	Not specified.	Different dental cements.	Resin-based cements stayed stable. Others changed more over time.
Radhakrishnan <i>et al.</i> (2023) [30]	To test sorption and solubility in water, saliva, and soda.	126 discs tested in 3 liquids over 5 weeks, with weight tracking.	42 per material (GIC, RMGIC, resin cement).	GIC, RMGIC, Resin Cement.	Resin cement was the most stable. GIC and RMGIC had more solubility, especially in acidic media.
Leal <i>et al.</i> (2016) [32]	To test how ceramic translucency affects cement water uptake.	ISO 4049-based test under different ceramic laminates.	Not specified.	Resin-based and other luting cements.	More translucent ceramics increased sorption/solubility. Resin-based cements were more stable.
Bharali <i>et al.</i> (2017) [34]	To test cements in artificial saliva of different pH levels.	Immersion in pH 5 and 7 saliva, following ISO protocols.	Not specified.	4 luting cements (not all named).	Resin-based had lower values. Acid increased degradation, especially for glass ionomer cements.
Ülker <i>et al.</i> (n.d.) [35]	To test the cytotoxicity of temporary cements using pulp cells.	Used 2D & 3D cell cultures; viability measured after cement extract exposure.	Bovine dental pulp cells.	Temporary luting cements.	Some cements were more toxic, especially in the 3D model. More realistic testing is needed.
Shams <i>et al.</i> (2024) [36]	To evaluate the mechanical properties of BioCem® vs Fuji I® (shear and flexural strength).	Shear bond strength was tested with a universal testing machine; flexural strength with standardized specimens.	60 extracted deciduous molars.	BioCem® (dual-cure, universal, bioactive), Fuji I® (conventional GIC).	BioCem® had higher flexural strength than Fuji I®. BioCem® had lower shear bond strength than Fuji I®.

Risk of bias assessment

Table 2. Risk of bias assessment of all the included studies

Study	Sample Preparation & Standardization	Randomization of Specimens	Blinding	Controlled Variables (pH, temp)	Data Reporting	Statistical Analysis	Conflict of Interest	Overall Risk of Bias
Gerdolle <i>et al.</i>	Yes (ISO 4049)	Not stated	Not	Yes	Adequate	Basic	Not	Moderate

(2008)			mentioned			(Descriptive only)	reported	
Yoshida <i>et al.</i> (1998)	Yes	Not stated	Not mentioned	Yes (2 media types)	Adequate	Limited	Not reported	Moderate
Gavranović-Glamoč <i>et al.</i> (2020)	Yes (ISO 4049:2009)	Not stated	Not mentioned	Yes (pH 3.0 & 7.4)	Good	Yes (Mann-Whitney U Test)	Not reported	Low
Kwon <i>et al.</i> (2015)	Yes (Cell culture methods described)	Not stated	Not mentioned	Partially controlled	Good	Yes	Not reported	Moderate
Jamel <i>et al.</i> (2020)	Yes	Not stated	Not mentioned	Yes (Time intervals monitored)	Adequate	Limited	Not reported	Moderate
Radhakrishnan <i>et al.</i> (2023)	Yes	Yes	Not mentioned	Yes (3 media types)	Good	Yes	Not reported	Low
Leal <i>et al.</i> (2016)	Yes (ISO 4049)	Not stated	Not mentioned	Yes (ceramic translucency)	Good	Yes	Not reported	Low
Bharali <i>et al.</i> (2017)	Yes	Not stated	Not mentioned	Yes (pH 5 & 7)	Adequate	Yes	Not reported	Moderate
Ülker <i>et al.</i> (2013)	Yes (2D & 3D cultures)	Not stated	Not mentioned	Yes	Adequate	Yes	Not reported	Moderate
Shams <i>et al.</i> (2024)	Yes (randomized groups, machine-tested)	Yes	Not mentioned	Yes (uniform testing)	Good	Yes	Not reported	Low

Examining the potential risk of bias in the included in-vitro studies, factors such as sample preparation, standardization of testing protocols, statistical evaluation, and overall reporting transparency were analyzed. The majority of studies adhered to ISO 4049 or ADA standard testing procedures, which aids in the consistency and comparability of the studies. However, some studies did not provide detailed descriptions of randomization and blinding, which, while neglected in in vitro studies, is still capable of introducing performance or detection bias (**Table 2**).

Gerdolle *et al.* (2008) presented a moderate risk of bias due to a lack of operator blinding and random allocation, resulting in imprecise measurement objectivity [20]. These authors, along with others, disregarded reporting operator blinding, which enhanced skepticism regarding measurement objectivity. Although these authors followed ISO standards and reported all experimental steps, their lack of detail surrounding operator blinding and random specimen allocation diminishes measurement objectivity. Similar to these findings were Yoshida *et al.* (1998) [21], where the lack of blinding alongside unclear sample preparation introduced moderate bias despite the use of an ADA modified protocol, suggesting methodological reliability.

Gavranović-Glamoč *et al.* (2020) and Radhakrishnan *et al.* (2023) performed studies that showed low to moderate risk [22, 30]. The studies followed ISO 4049:2009 guidelines

and published detailed sample sizes, rigorous statistical analyses, and provided a thorough methodology. However, their lack of mention of randomization or blinding procedures creates the possibility for performance and detection bias. Kwon *et al.* (2015) [25], including cell culture testing for biocompatibility in shields, applied advanced cytokine analysis, which enhanced biological relevance. Even so, there was no mention of blinding in the cytokine quantification, nor clarity in the sample selection, leading to a moderate risk of bias.

Jamel *et al.* (2020) and Leal *et al.* (2016) also followed set ISO standards that emphasized meticulous methodology [28, 32]. However, the studies lacked clarity on operator bias and allocation concealment, leading to a moderate risk rating. Bharali *et al.* (2017) also followed ISO standards and described closely controlled environmental conditions [34], including controls and test parameters. Still, the sparse description of how specimens were allocated to test groups suggests potential allocation bias.

The research conducted by Ülker *et al.* (2013) investigating the cytotoxic effects of certain agents on 2D and 3D pulp cell cultures provided a stronger model of in vivo conditions than previously achieved [35]. Regardless, the study had no blinding, ambiguous data on how extract concentrations were standardized, and a moderate risk of bias. Shams *et al.* (2024) complemented extracted teeth with more vigorous mechanical testing, proper use of control groups [36], and

uniform measurements. Still, the lack of randomization and blinding of the outcome assessment described puts the study in the moderate risk tier.

The functional effectiveness and longevity of dental restorations greatly rely on the properties of the luting cements used. As the materials forming the bonding interface between the tooth structure and the restoration, their function is governed by water sorption, solubility, biocompatibility, and mechanical properties. This analysis incorporates recent studies on luting cements in relation to previously conducted research in order to analyze their behavior in different conditions and the implications for clinical work.

Water sorption and solubility

Currently available research has shown resin-based luting cements such as Variolink II and Panavia F have significantly less water sorption and solubility in comparison to RMGICs like Fuji Plus and polyacid-modified Resinomers. For example, Gerdolle *et al.* (2008) reported that Fuji Plus had high water sorption and solubility [20], which supports the material's hydrophilic nature as well as the acid-base reaction setting mechanism employed. Although Resinomers exhibited higher water sorption and solubility than other resin-based cements, they were still lower than that of Fuji Plus. Variolink II and Panavia F yielded low values, and thus had better resistance to water uptake and dissolution. These findings resonate with previous research, such as Taher and Al-Zubaidi (2020) [37], who noted conventional GICs degrade over time due to a porous structure containing hydrophilic components that absorb water. Kamseu *et al.* (2021) [38] further supported this by associating greater porosity in GICs with increased water uptake, thus weakening the material. Water sorption is lower in resin cements because of dense polymer networks and hydrophobic monomers, as described by researchers [39, 40].

Another important factor is the effect of pH on water sorption and solubility. The oral cavity is particularly prone to pH changes as a consequence of food intake, bacterial metabolism, or pathological conditions. An increased acidity region can make the material more soluble and prone to degradation. Conventional and resin-modified GICs are significantly more soluble in acidic conditions than neutral ones to Yoshida *et al.* (1998) and Gavranović-Glamoč *et al.* (2020), while resin cements showed greater stability [21, 22]. Radhakrishnan *et al.* (2023) [30] confirmed this by showing the least solubility of resin cement in distilled water, artificial saliva, and carbonated water, while GICs and RMGICs were more prone to acidic media.

These conclusions align with Silva *et al.* (2021) [41], which showed greater GICs solubility in acidic conditions as well as diminished mechanical properties. Moshaverinia *et al.* (2018) [42] also demonstrated that the addition of resin components into GICs diminishes clinical performance

through lowered solubility and water sorption. All these findings, taken together, clearly indicate that resin cement is a better material choice for patients with acidic oral environments or high moisture exposure because it is less soluble and more resistant to water. The susceptibility of GICs and RMGICs to these types of degrading conditions, however, poses concerns regarding their long-term durability.

Biocompatibility

Kwon *et al.* (2015) used cytokine release assays to study the inflammatory response of human oral fibroblasts and keratinocytes to the extracts of various luting cements [25]. This approach goes beyond biocompatibility evaluation through MTT assay, providing enhanced detail on biocompatibility. The findings showed that most cements tested were non-cytotoxic in MTT assays, but some showed different levels of cytokine release and hence divergent inflammatory potential. This level of detail aids the understanding of the extent to which materials may induce inflammation in surrounding tissues in vivo.

Cumulative evidence strengthens these findings. Schmidlin *et al.* (2017) [43] also demonstrated that material-tissue interaction assessment through cytokine profiling is more advanced than other methods. In their study, Attik *et al.* (2015) [44] reported that resin cements with 10-MDP functional monomers typically released less inflammatory cytokines and posed lower inflammatory responses than zinc phosphate and GICs. Further, Koulaouzidou *et al.* (2009) [45] reported that GICs would tend to release fluoride and other ions, which would initiate the proinflammatory mediators that could, in turn, irritate the tissues. Therefore, for optimal mechanical retention, resin-based luting cements like Variolink II and Panavia F provide superior mechanical retention while having fewer inflammatory responses. This makes these materials more appropriate where soft tissue inflammation would render dental care intervention difficult in the gingival areas.

On the other hand, the cytotoxic effects of temporary luting cements have been inconsistent. Ülker *et al.* (2013) investigated cytotoxicity using 2D and 3D cultures of bovine dental pulp cells and noted greater cytotoxicity in 3D cultures, which more closely represent natural tissue surroundings [35]. This highlights the need to design temporary cements that are more biocompatible to preserve the health of the dental pulp during temporary restorations.

Mechanical properties

The recent study by Shams *et al.* (2024) focuses on the evaluation of a new bioactive dual-cure cement, BioCem® [36], in comparison with the conventional glass ionomer cement Fuji I®. It was found that BioCem® exhibited superior flexural strength and lower shear bond strength. This means that BioCem® is better at enduring bending forces, but the ability to bond to tooth structures is weaker; therefore, the clinical applicability is limited unless

improved adhesion is developed.

These findings correlate with those of Prati *et al.* (2014) [46], who observed the phenomenon in bioactive materials where internal strength due to the mineral ion release and remineralization significantly increased, but surface bonding was impaired. Abed *et al.* (2023) [47] showed that surface treatments and primers greatly enhance the bond strength of resin cements, which emphasizes the need for uniform cementation protocols, especially with newer bioactive cements. Braga *et al.* (2020) [48] and Chutinan *et al.* (2005) [49] corroborate these findings. They reported that GICs suffer from an increase in solubility and water uptake over time. Still, the strength of resin-based cements is retained, supporting their use in long-term restorations.

Environmental factors and clinical implications

Multiple studies recently focused on the impact of pH on solubility and sorption [21, 22, 25, 28]. Lower pH increases the erosion of GICs and RMGICs since these materials are more sensitive to acidic conditions. On the other hand, resin cements are more stable with changes in pH, which is beneficial for patients suffering from GERD or other conditions that lower the oral pH, such as high-sugar diets. Leal *et al.* (2016) [3] analyzed the effect of the degree of translucency of a ceramic restoration on water sorption. They concluded that ceramic translucency, indeed, affects water sorption and the solubility of the cementing luting agents underneath the ceramic. Underlying opaque resins were less impacted, indicating that they could be placed beneath various ceramic restorations without compromising their longevity.

These are its clinical aspects that are undeniable. In determining the best luting agents, dentists need to pay attention to the oral cavity's environment in terms of pH, diet, and the restoration type. Water-soluble resin cements sustain less water sorption, solubility, and inflammatory damage, so they are the most common choice. GICs and RMGICs might be used in some situations where fluoride release or chemical adhesion is needed; thus, clinicians need to consider the sensitive nature of these materials in moist or acidic environments.

Research limitations and future directions

Thermal cycles in laboratories that are eutectically controlled, simulating the oral cavity, have multiple external variables such as enzymes, bacteria, and mechanical stress that are yet to be studied. These factors need further thorough examination. Furthermore, there is a clinical gap in longitudinal studies evaluating the performance of the products used in laboratory tests.

The behaviors of glass ionomer cements modified with resins during changing and simulated oral environments especially need to be studied further. Also, the effects of saliva, the oral microbiome, and their other constituents in cementing material used in luting need to undergo additional

detailed study. Other investigated factors have more than enough research material focused on them—cementing material needs to be biocompatible, active, mechanically resistant, and strong to withstand the physiological environment. Also, other bioactive materials like BioCem® require other detailed standardized bioactive material cementation techniques detailing how to enhance bond strength and amplify clinically determined success rates reliably. Clinical trials involving profiling of cytokines also need further examination for inflammatory response measuring and associative biocompatibility assessment in various luting cementing materials.

Conclusion

Based on the systematic review, resin-based luting cements, both self-adhesive and dual-cure types, dominate other materials in the areas of biocompatibility with the pulp and solubility of composite resin luting cements. They are, therefore, a more dependable option for sustained retention in fixed prosthodontics. These materials exhibit low inflammatory response as well as lower degradation due to moisture and acid exposure, which are prevalent in the oral cavity.

In contrast, the biocompatibility of resin-modified glass ionomer cements is generally lower due to higher solubility, increased biocompatibility variability, particularly in acidic environments, and concerns regarding pulpal irritation alongside restoration durability. Taking into consideration the clinically relevant issue of preserving the integrity of the restoration while safeguarding pulpal health, it is advised to utilize resin-based luting cements for indirect restorations in the Saudi dental context.

Acknowledgments: We would like to acknowledge the research center of Riyadh Elm University.

Conflict of interest: None

Financial support: None

Ethics statement: None

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