ORIGINAL ARTICLE

Rheological and Mechanical Evaluation of Metformin-Modified Dental Restorative Glass Ionomer Cements (GIC): A Preliminary In-Vitro Study

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Abstract

Background: Glass ionomer cements are being widely used in dentistry, with the incorporation of pharmaceutical agents enhancing their physical properties.

Objective: The objective of this work was to assess the mechanical and setting characteristics of metformin-modified glass ionomer cement (GIC) restorative materials**.**

Materials and Methods: The research design adopted for this study was an in-vitro experimental study involving the testing of two types of restorative glass ionomer cements (GICs), FUJI and 3M Ketac Molar, with concentrations of 0%, 1.5%, 3.0%, and 4.5% metformin hydrochloride (MF). The control group (CG) consisted of a conventional GIC without MF. Fourier Transform Infrared (FTIR) spectroscopy was used to characterize the sample. Flexural strength (FS), tensile strength (TS), and Vickers microhardness testing were used to analyze mechanical properties, and the Vicat test was used to examine setting behavior. Statistical analysis was conducted using two-way ANOVA.

Results: It was observed that 3M Ketac Molar groups showed higher FS and Vickers microhardness values than FUJI IX groups. 3M-CG had maximum microhardness (69.0 ± 0) and FS (48.0 ± 1), while FUJI + MF 4.5 wt% had lowest values (61.0 ± 1.4 and 33.6 ± 1.3). Mean TS values of 3M groups exceeded those of FUJI groups, except for FUJI with 3% and 4.5% MF. 3M-CG had highest TS (23.0 ± 0), and 3M + MF 4.5 wt% the lowest (11.2 ± 1.5).

Conclusion: The inclusion of metformin in GIC caused a reduction in the mechanical and setting properties of the GIC in relation to the concentration level, with comparatively less change at 1.5 wt.%. Further biological and clinical studies are required.

Keywords: *Glass Ionomer Cements, Metformin, Mechanical properties, Setting properties.*

Introduction

Dental caries is among the most common diseases worldwide, which damages the mineralized tooth structure, causing extensive destruction, pain, and increased susceptibility to further damage.[1] Deep restorations can irritate the pulp, leading to pulpitis or necrosis. These challenges are not fully addressed by current restorative treatments. Ideally, restorative materials should replace lost tooth structure as well as promote dentin remineralization, pulp healing, and regeneration.[2]

Glass ionomer cement (GIC) is a self-adhesive cement that chemically bonds to the tooth structure [3]. GICs are commonly employed for luting, lining and base, restorative/filling materials, and atraumatic restorative treatment (ART), particularly in pediatric patients.[4,5] It is available in powder and liquid form, which must be combined by hand. The liquid component is polyacrylic acid, and the powder component is fluoro-aluminosilicate glass. Combining GIC's liquid and powder results in an acid-base reaction.[6,7] Their biocompatibility, antibacterial activity, sustained fluoride release, low thermal coefficient of expansion identical to that of teeth, and ability to bond make GIC popular in dentistry.[8–10] In addition, the cement can also be recharged with fluoride ions in the oral cavity.[11] Despite various merits, GIC has very limited potential to be used as a regenerative material in deep carious lesions. The ideal material for deep carious lesions or vital pulp capping should possess the ability to stimulate the remaining pulp tissue to return to its normal condition to promote dentin formation.[12]Metformin hydrochloride (MF) is a first-, generation biguanide medication for type 2 diabetes. Since it has good tolerance

low cost, safety, and non-toxicity, the drug is highly used to control blood sugar in type 2 diabetes.[13] Studies have shown that metformin stimulates the production of pre-osteoblasts and bone marrow mesenchymal stem cells (MSCs), both of which have an osteogenic effect.[14, 15] By activating the AMP-activated kinase (AMPK) signaling pathway, metformin can promote pre-osteoblast differentiation and mineralization into osteoblasts. Via the liver kinase B1 (LKB1)/AMPK signaling pathway, it stimulates the mineralization of pluripotent stem cell-derived MSCs (iPSC-MSCs) and initiates osteogenic differentiation, thereby repairing and regenerating bone.[16,17] Based on clinical studies, topically applied metformin can induce regeneration of the periodontal bone. Intracanal MF reduced bone loss, enhanced osteoblast differentiation, and decreased osteoclastogenesis in rats with apical periodontitis.[18] Wang et al used resin as a carrier agent to deliver metformin locally to stimulate dental cells for dental tissue regeneration and discovered that dental pulp stem cells (DPSCs) proliferation was 4 times higher on metformin-containing resin than on control.[19] Yu et al used resin specimens with different concentrations of metformin to evaluate its effects on the osteogenic and cementogenic differentiation of human periodontal ligament stem cells (hPDLSCs) and discovered that the MF group had cementogenic and osteogenic differentiation values that were 2.5 and 2.3 times higher, respectively, than the control without metformin ($p < 0.05$).[20] Another study revealed that metformin, AMPK-dependently, can enhance mineralization and differentiation of dental pulp cells (DPCs). This has implications for regenerative endodontics and other regenerative uses, suggesting that this well-tolerated antidiabetic drug can be employed[21] as shown in Figure 1. Previous research has studied the effect of antibiotics, clay, and nanoparticles, etc., to enhance the properties of GIC; however, the effect of MF on the mechanical and setting properties of GIC has not been studied before. Therefore, this study aims to evaluate the effect of MF incorporation into GIC on the mechanical and setting properties of GIC. The objective of this study is to assess the mechanical and setting characteristics of metformin-modified glass ionomer cement (GIC) restorative materials.

Materials and Methods

Formal ethical approval was waived, and an institutional exemption wasgranted (Ref. No.: Ref No: IRB-3892/DUHS/Approval/2025/186

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because the study exclusively evaluated synthetic, non-biological dental materials and involved no human participants, animal subjects, or human tissue specimens. This experimental in-vitro study utilized two brands of GIC, i.e., FUJI (GC Corporation) and 3M Ketac Molar (3M ESPE, 3M Company) restorative GIC. The antidiabetic drug metformin hydrochloride powder form (SHOUGUANG FUKANG PHARMACEUTICAL CO. LT.) was incorporated and mixed into the powder of conventional GIC on a mixing pad in 1.5wt %, 3.0 wt%, and 4.5 wt% concentrations. The GIC powder and liquid were combined in a ratio of 3.6:1, according to the instructions of the manufacturer. The nominal ratio was applied for both the control samples and those treated with metformin. Nevertheless, the addition of metformin resulted in a change in the composition of the powder, possibly affecting the ratio of GIC components. Samples were covered with polyester strips for seven minutes until initial reaction completion and removed using tweezers.

The study included two GIC brands (FUJI and 3M Ketac Molar) and four formulations for each brand: control (0%), 1.5 wt%, 3.0 wt%, and 4.5 wt% metformin hydrochloride. A total of 40 specimens (5 for each group) were used for microhardness testing, and the same specimens were subsequently used for estimated tensile-strength calculation. A separate 40 specimens (5 for each group) were used for flexural-strength testing, while 80 specimens (10 for each group) were used for the Vicat test. The NCSS PASS version 15 software determined the sample size for both mechanical and setting tests Samples were stored in distilled water at 37ºC for 24 hours. Discs (10 mm diameter, 2 mm height) were used for Vickers micro-hardness, bar shaped (25 mm length, 2 mm height, 2 mm breath) for flexural strength, and discs (4 mm diameter, 1 mm height) for the Vicat test.

The characterization of control and test samples was done by crushing the discs in a mortar and pestle. The powdered discs were then analyzed using Fourier-transform infrared spectroscopy (FTIR) (Thermo Scientific Nicolet iD7 ATR, USA) and Ominic (version 9.0) software with the wavelength range of 4000-700 cm -1, which is a device used to identify the 'fingerprint' of substances to determine their identity, quality, and impurities [21]. The functional groups in materials give rise to characteristic bands that help identify the chemical nature of the substance[22].

For Hardness samples were prepared using circular stainless-steel molds. The Vickers microhardness tester (HMV-7000, Shimadzu) was used. Vickers diamond indentations were performed for 15 seconds under 100 g force, with three indentations per specimen to obtain an average. After measuring diagonal length imprints, the hardness number H was determined using the conventional formula:

$H = 1.854\ P/d.^2$

H: Microhardness value showing resistance to indentation.
P: Applied load during the test (in kg or N).
d: Mean diagonal length of the indentation (in mm).
1.854: Constant based on the Vickers indenter geometry.

For flexural strength specimens were created using stainless steel molds and then subjecting samples to a 3-point bending test at a crosshead speed of 1 mm/min. The samples were loaded on the Universal Testing Machine (Instron, High Wycombe, UK) with a 1 kN load until they fractured. The formula for calculating flexural strength (σ) is:

$\sigma = 3Fl / 2bh^2$

Where b = specimen's breadth (2 mm), h = height (2 mm), l = distance between the supports the sample is situated on (20 mm), and F = maximum load (FN).

Tensile strength was estimated from the Vickers microhardness values obtained from the specimens used for hardness testing. Mean hardness was estimated for the three specimens per group after Vickers indentation using the following empirical equation:

$\sigma UTS = HV/3.34 - 56$[23]

Where σUTS represents the estimated ultimate tensile strength, and HV represents the Vickers hardness value. The calculated values were therefore treated as hardness-derived estimates of tensile strength rather than direct experimental tensile-strength measurements.

Setting time setting measured through the use of a Vicat needle test carried out under specific conditions. Samples were placed on a glass plate soon after mixing, kept at 37 °C temperature and 90% relative humidity. Following 90 seconds, a Vicat needle (Stanhope Seta Limited, England; 1.0 ± 1 mm diameter; 300 ± 5 g) was applied for 6 seconds at 30-second intervals. Time setting was calculated in minutes beginning from the end of the mixing process to the time when the needle did not make any complete circular impression. [24] This test was done for all samples. FUJI 4.5 wt% metformin group exhibited a time-setting value of 0.46 ± 1.60 min. After mechanical and setting testing, the data were statistically analyzed using SPSS for Windows version 16. Two-way analysis of variance (ANOVA) was used to evaluate the effects of GIC brand and metformin concentration, as well as their interaction, on the measured outcomes. The least significant difference (LSD) post-hoc test was used for pairwise comparisons where significant differences were identified. Statistical significance was set at $p < 0.05$.

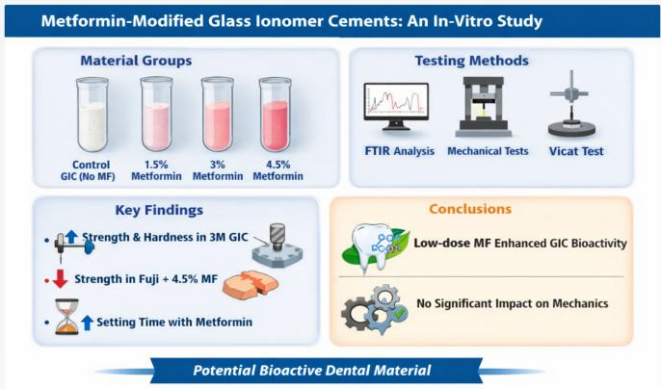

Figure 1: Graphical Abstract

Results

FTIR spectroscopy showed the initial notable peak is observed at 3749.8 cm-1, indicating the presence of hydroxyl (OH-) groups (3200–3600 cm^{-1}), which are likely linked to the water content in the material. The second peak at 1062.35 cm-1 is indicative of phosphate or silicate groups in the material. These groups are essential for the GIC's ion-releasing and tooth-adhesion properties.. A peak at 731.28 cm^{-1} is likely due to the stretching vibrations of Si-O or P-O bonds in the glass phase, which significantly influences the cement's mechanical properties. Two peaks are observed at 1698.86 cm^{-1} and 1510.87 cm^{-1}. These represent the carbonyl group (C=O stretching (1650–1750 cm^{-1})), indicating the presence of metformin in the sample. FTIR analysis of FUJI and 3M Ketac Molar GICs having 1.5, 3.0, and 4.5 wt.% of metformin hydrochloride. FTIR spectra show absorption bands within the analyzed range of wavenumbers, along with distinct sections emphasizing some notable spectral peaks. Similar spectral patterns for all the formulations imply equal chemical properties after metformin addition. as shown in Figure 2.

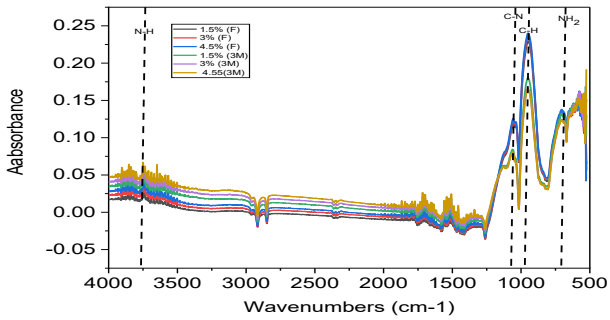

Figure 2: Graphical representation of GIC (Fuji & 3M) + metformin using FTIR.

Table 1: Mechanical & Setting Properties comparison within Concentration.

Mechanical & Setting Properties	0% (Control) (N = 50)	1.5% (N = 50)	3% (N = 50)	4.5% (N = 50)	P-value[¥]
Microhardness (MPa)					
FUJI	67 ± 0	65.2 ± 0.8	63.2 ± 0.8	61.0 ± 1.4	<0.001
Comparison with Control[a]	-	1.8 (0.049)	3.8 (<0.001)	6.0 (<0.001)	
3M	69.0± 0	67.1± 0.9	64.8± 0.9	62.2± 0.9	
Comparison with Control[a]	-	1.8 (0.049)	4.1 (<0.001)	6.8 (<0.001)	
Flexural Strength (MPa)					
FUJI	41.00± 0	38.60± 0.7	36.00± 0.7	33.60± 1.3	<0.001
Comparison with Control[a]	-	2.4 (0.001)	5.0 (<0.001)	7.4 (<0.001)	
3M	48.0± 1	45.6± 0.2	42.0± 0.3	38.40± 1.2	
Comparison with Control[a]	-	2.4 (0.001)	6.0 (<0.001)	9.6 (<0.001)	
Tensile Strength (MPa)					
FUJI	20.0± 0	18.4± 0.2	16.0± 0.2	12.6± 1.3	
Comparison with Control[a]	-	1.60(0.011)	4.0 (<0.001)	7.4 (<0.001)	<0.001
3M	23.0± 0	20.0± 0.9	15.4± 0.9	11.2± 1.5	
Comparison with Control[a]	-	3.0 (0.001)	7.6 (<0.001)	11.8 (<0.001)	
Setting Time (seconds)					
FUJI	2.0± 0	1.4± 0.4	1.2± 0.4	.46± 1.6	<0.001
Comparison with Control[a]	-	.59 (0.05)	.75 (<0.001)	1.5(<0.001)	
3M	5.0± 0	3.2± 0.8	1.6± 0.9	1.0± 1.4	

a = Comparison with control (conventional GIC)

[¥]Two Way ANOVA with Post Hoc (LSD) test. All values are presented as mean ± standard deviation, [a] Values presented as mean difference (p-value).

The results of this study indicate that when MF was incorporated into Fuji and 3M Ketac Molar all the properties deceased as indicated in Table 1. The table shows comparisons of microhardness, flexural strength, estimated tensile strength, and setting time for control (0%) and metformin (1.5%, 3.0%, and 4.5%). The differences between the mean values compared to respective controls are shown with p-values. Two-way ANOVA with LSD post-hoc test was performed, where $p < 0.05$ is taken to be statistically significant.

Discussion

FTIR spectroscopy is a non-destructive technique used for the analysis of various substances, including chemicals, biological samples, and pharmaceuticals.[25] it indicates chemical alteration in the material, as new bands appear in the absorption spectrum due to possible changes.[26] The metformin-modified GIC analysis provides crucial insights into the molecular structure of the composite material. Several peaks appear at specific wavelengths, each corresponding to a different functional group. The chemical nature of the drug remained unchanged across all concentrations, further supporting the assumption that adding metformin to GIC does not compromise the drug's chemical properties. This highlights that at specific concentrations, metformin could be incorporated into dental cements.

Hardness is the ability of a material to withstand plastic deformation, which is usually determined under an indentation load. It is one of the most significant properties that reflects the clinical durability of dental materials.[27-28] The results of this study indicate that when MF was incorporated into Fuji and 3M Ketac Molar GICs, hardness decreased. It was observed that surface microhardness decreased with increasing drug concentration, with samples containing 4.5% MF exhibiting the lowest microhardness values. The mean microhardness values of all 3M Ketac Molar groups were significantly higher than those of their corresponding FUJI GIC groups. A significant difference in microhardness was observed between the modified and unmodified GIC groups (p-value < 0.001). Previously conducted studies have shown that incorporating drugs, such as antibiotics, into GIC affects its physical and setting properties, either increasing or decreasing them, while at some concentrations the properties remain unchanged. Changes in GIC's cross-linking brought on by the addition of a medication are responsible for the altered characteristics. These alterations prevent several COOH groups from taking part in the interaction between Al^{3+} and Ca^{2+} and the COOH groups present in acidic polymers. Consequently, the hardness of GIC decreases[28]. Medicines and other compounds can absorb water molecules and affect cement hardness. These changes may also be related to changes in the powder-to-liquid (P/L) ratio of GIC when they are added to the powder. According to a study, the antibacterial and fluoride-releasing capabilities of restorative materials were enhanced by adding a 1% antibiotic mixture of ciprofloxacin and metronidazole, without affecting their mechanical properties.[29] Another study showed that as antibiotic concentration increased, the contact of glass particles in GIC decreased. This implies that when metformin is increased it could decrease the mechanical properties. Therefore, this study corresponds to what is already been discovered in open literature. However, at very low concentration of the drug, the properties are somewhat unchanged. This is consistent with the findings of our investigation. This implies that diabetic dental patients may benefit from such low MF concentrations.

Flexural strength of a material is an indicator of resistance to fracture under functional loads during mastication[30]. Hiremath et al stated that the most appropriate measure of GIC's strength is obtained by the flexural test [31]. In this study, Flexural strength (FS) was assessed to better understand the performance of MF-modified GIC in clinical practice. It was observed that the flexural strength of MF-modified samples decreased with an increase in drug concentration, with the lowest values of flexural strength observed in samples with 4.5 wt % MF. Furthermore, statistical analysis showed that the mean flexural strength values of all 3M Ketac Molar GIC groups were significantly higher in comparison to their corresponding FUJI GIC groups. With a p-value < 0.001, a significant difference was observed in the flexural strength of GIC groups with increasing concentrations of MF. One study demonstrated that incorporating the penicillin group into restorative GIC material influenced the physical properties of GIC at some concentrations, whereas they remained unchanged at others. The changes in properties after drug addition can be attributed to the inhibition of the coordination of COOH groups with Al3+ and $Ca2^{+,}$ which compromises the FS of the modified GIC [32]. Another reason for the change in FS after drug addition could be the absorption of water molecules by these drugs, which can, in turn, affect the P/L ratio. Furthermore, high concentrations of drug in GIC can interfere with the interaction between glass particles and liquid, which is consistent with the results observed in our study.

TS test is one of the frequently used methods for evaluating the mechanical properties of a new dental cement. TS of restorative materials is an important property that determines their durability during function. This test could be used to determine the brittleness of dental materials [33, 34]. The Tensile strength of the samples was

calculated using hardness values. It was observed that the tensile strength of the samples decreased with increasing MF concentration, with the lowest tensile strength observed in samples containing 4.5 wt % MF. However, minimal change was noticed at 1.5 wt. %. Statistical analysis showed that the mean tensile strength values of all 3M Ketac molar GIC groups were significantly higher than those of their corresponding FUJI GIC groups, except for the 3 wt % and 4.5 wt % MF groups, which showed the opposite result. With a p-value < 0.001, there is a significant difference in tensile strength across GIC groups with increasing MF concentration. This change in tensile strength could be attributed to a change in the P/L ratio, interference of the drug with glass particles- liquid interaction, or inhibition of coordination of COOH with Al^{3+} and Ca_2^{+} as discussed previously. However, no significant difference is observed between conventional GIC groups and the 1.5 wt% MF-modified group. This suggests that the low concentrations of MF could be useful for diabetic dental patients.

Rheology is the science of the flow and deformation of materials, which interrelates time, force, and deformation [35]. An important setting property of dental cements is setting time, which is defined as the time from the completion of the mixing process until the cement hardens. The setting reaction of GICs has been extensively studied and depends on their composition and the environment [36]. Dental cements need to have an ideal setting time that is neither too short nor too long. A setting time that is too short would mean the dentists would not have enough time to manipulate it, while a setting time that is too long would mean the patients would have to wait in the clinic for a longer time [37]. According to the manufacturer, the setting time of Fuji restorative GIC is 2 - 3 minutes. GIC modifications are known to improve the setting response, compromising the handling qualities of these materials [38, 39].

The study's findings demonstrated that the setting time of modified GIC decreased as the MF concentration increased. According to statistical analysis, all 3M Ketac molar GIC groups had considerably longer mean setting times than their respective FUJI GIC groups. With a p-value < 0.001, a significant difference exists in the setting time of GIC groups with an increase in MF concentrations. As a result, the P/L ratio affects the GIC setting time. The release of MF from GIC or the synergistic relationships between the MF and GIC may be the cause of the reported reduction in the setting time of MF-modified GIC (Fuji and 3M Ketac Molar). Prior research has shown that the setting time of conventional GIC is impacted by the inclusion of medications or bioactive substances, such as chlorhexidine. Because of the presence of cationic quaternary ammonium compounds (such as cetylpyridinium chloride and benzalkonium chloride), which may have hampered setting mechanisms such as proton attack and ion discharge from glass particles, it was reported that chlorhexidine-modified GIC had a longer working time. According to another study, adding organic substances such as methanol and 2-hydroxyethyl methacrylate (HEMA) decreased both the rate and mechanical properties of the setting reaction.

One of the limitations of this current research is that there was no pure metformin control or an inert powder control available. Hence, the research was able to compare the properties of metformin-modified GICs and their respective unmodified GIC controls, but it was unable to separate the effect of metformin from the powder additive completely. It is recommended that future researchers use inert powder and metformin-only controls for their research purposes.

Similar to mechanical qualities, the setting characteristics of GIC can be impacted by pharmacological interference with the glass-liquid interface or by suppression of COOH coordination with Al^{3+} and Ca^{2+}. Furthermore, it is recommended to study the regenerative response of the MF-modified GIC. Moreover, further characterization (such as SEM and XRD) is required to investigate the potential of this modification. With the possible involvement of metformin in the regeneration of bone and dental tissues, the MF-GIC could be used in the future in patients suffering from diabetes or having bone problems. Nevertheless, more research should be carried out to see if there is any clinical benefit from these possible applications.

Conclusion

Results revealed that metformin hydrochloride addition had an effect on the mechanical and setting behaviour of GIC. Micro-hardness, flexural strength, estimated tensile strength, and setting time reduced in relation to the metformin concentration. 1.5 wt.% formulation changed less when compared to other concentrations. Hence, metformin-modified GIC offers a promising bioactive alternative for restorative dentistry, mainly for diabetic and bone-compromised patients.

CONFLICT OF INTEREST: None

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Author Contributions

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2. Ashfaq Ahmed: Literature search, data curation, writing - original draft, and visualization.
3. Tuba Shakeel: Writing - original draft, review, and editing.
4. Arshad Hassan: Literature search, writing, and review.
5. Muhammad Ali Siddique: Review and editing, and formal analysis.
6. Ambreen Murtaza: Quality assessment, writing - review and editing.
7. Mah Zul Kaif: Data curation and editing.