

Surface Roughness Examination of Glass Ionomer Restorative Cements Treated with Acidic and Basic Pediatric Medications: An *In Vitro* Study

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ABSTRACT

Background: Consumption of different types of beverages and liquid drugs can affect of the surface properties of restorative material. This may lead to an increased probability of dental caries and periodontal inflammation. **Aim:** This study evaluated and compared the effect of amoxicillin suspension (AMS) and azithromycin suspension (AZS) on the surface roughness (SR) of silver-reinforced glass ionomer (SGI) and nano resin-modified glass ionomer (NGI). **Material and Methods:** Thirty disks (2mm height × 4mm diameter) of each glass ionomer (GI) type were prepared and subdivided into three groups ($n = 10$), which were separately exposed to AMS, AZS, and artificial saliva (AS). SR was evaluated by atomic force microscopy before and after three-immersion protocols repeated over a 3-week duration with 2-day intervals. In each protocol, the GI samples were exposed weekly to AMS three times daily, AZS once daily, and a full day to AS. **Results:** This study demonstrated, for the first time, the effect of a basic drug (AZS) on the SR of GIs. Intra- and inter-group comparisons showed significant changes ($P < 0.05$) in the SR pattern of the GIs after immersion cycles in AZS, AMS, and AS. However, the acidic medication (AMS) exhibited significantly higher changes in SGI than in NGI. **Conclusions:** The SR of NGIs and SGIs can be significantly affected by the use of AMS and AZS suspensions. SGI demonstrated higher SR deterioration than NGI after immersion cycles in AMS.

KEYWORDS: Amoxicillin suspensions, antibiotic, azithromycin suspension, medicines, nano resin-modified glass ionomer, silver-reinforced glass ionomer, surface roughness

INTRODUCTION

The use of liquid medications to treat conditions such as microbial infections and pain during childhood can have adverse effects on the restoration/prosthesis present inside the oral cavity.^[1] Among these medications is the amoxicillin suspension (AMS), a type of penicillin (B-lactam) antibiotics^[2] that is widely prescribed in dental practice for its effectiveness in treating various kinds of oral infections.^[3] In cases of possible allergic reactions to AMS, azithromycin suspension (AZS) is indicated as an alternative. In comparison to AMS, AZS has the same antibacterial

spectrum, however, the latter can be administered once daily in comparison with thrice per day use of AMS.^[4-6] In pedodontics, glass ionomers (GIs) have wide and frequent clinical implementations due to the possibility of modifying and improving their physical properties.^[7] Attempts were conducted to enhance the mechanical properties of GIs via incorporating silver particles.^[8]

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However, the strength properties of silver-reinforced GI (SGIs) are still insufficient to withstand occlusal loads unless they are well supported by the surrounding tooth structure.^[7]

On the other hand, the incorporation of nanoparticles into micro-sized GI powder led to widened particle-size distributions, resulting in higher mechanical values than conventional GIs.^[9] Hence, nano resin-modified GI (NGI) could be a superior restorative material for dental applications.^[9]

Critical intraoral factors such as pH variation, humidity levels, as well as the intake of pediatric liquid medications could aggravate the biodegradation of restorative materials over time, leading to changes in their physical properties.^[10-12] A previous study reported that some liquid medications such as amoxiclav, metronidazole, cephalixin, ibuprofen and paracetamol affected the surface roughness (SR) of zirconomer, composite and GIs, in which the GIs demonstrated lower durability and higher SR changes in the immersion media as compared with other restorative materials.^[13] Moreover, a recent work studied the effect of multivitamin syrups on the SR and hardness of conventional GIs in comparison with resin-modified GIs. They demonstrated that the long term use of multivitamin solutions can adversely impact the physical characteristics of restorative materials.^[11] Thus far, no previous study has examined the effect of amoxicillin nor azithromycin suspensions (the regularly prescribed antibiotics for children) on the SR of NGI and SGI.

The rational of this study is that the difference in pH and chemical composition of AMS and AZS might exhibit different interactions with the chemical composition of NGI and SGI in terms of SR. So, the null hypothesis stated that there are no differences between the effect of AMS and AZS on SR of NGI and SGI; Therefore, this study aimed to assess the effect (and find the difference if any) of amoxicillin and azithromycin suspensions on the surface roughness of NGI and SGI samples.

MATERIALS AND METHODS

STUDY DESIGN

In *in vitro* study.

SAMPLE SIZE ESTIMATION

Sample size was estimated by G Power 3.1.9.7 (developed by Franz Faul, University of Kiel, Germany) with a statistical power of 80%, an alpha error probability (Type I error) of 0.05%, In addition, an effect size of F equaled to 0.40 (representing a large effect size) among 6 groups. The minimum required sample size was 60 (10 samples per group). Effect size F is accounted as: Small =0.1, medium=0.25, large=0.4.^[12,14,15]

BLINDING

The samples were randomly coded and blindly analyzed.

METHODS

This study was ethically approved by The Ethical Committee at the University of Baghdad College of Dentistry, Department of Basic Sciences (Reference number:573).

The mold was set on a transparent celluloid strip and secured on a glass cement slab. Afterwards, the GIs were applied and overladed with another matrix strip and glass cement slide, and 200 g pressure was used to remove surplus materials from the mold.^[16,17] Then, the specimen was directly applied to the top of a glass slide, light-cured (Germany’s Eighteenth model curing; LOT# G2108030) and polymerized as directed by the manufacturer.^[18] Another round of light curing (for 40sec) was applied to ensure the polymerization of the bottom of the GI discs.^[19] For standardization purposes, the GI discs were polished following a sequential polishing protocol used by Ibrahim *et al.* (2019).^[20] In 60 coded glass vials, 30 samples of each type of restorative material, NGI and SGI (Table 1) placed individually and coded depending on the type of GIs and the used medications [Figure 1]. For each kind of GI, the samples were subclassified into three groups (n = 10) and individually subjected to AMS, AZS, and artificial saliva (A.S).

Artificial saliva was prepared according to Björklund *et al.* The following materials were used to prepare one liter of artificial saliva: calcium chloride 0.05g, sodium fluoride 0.0002 g, magnesium chloride 0.05 g, potassium phosphate 0.04g, potassium thiocyanate

Table 1: Mode of activation, composition, and average particle size of GIs used in this study

Material	Mode of activation	Composition	Average particle size
NGI (3M-ES PE Ketac N100, St. Paul, MN, USA; LOT# NE60328)	Light cure	Monomers nanocluster, methacrylate modified polyalkenoic, HEMA(Hydroxyethyl methacrylate) FAS (fluoroaluminosilicate) and deionized water	Nanofillers 5–25 nm
SGI Riva sliver 8670008	Light cure	Sliver glass powder, acrylic acid, homopolymer, alloy powder, liquid acrylic acid homopolymer, and tartaric acid	8 μm

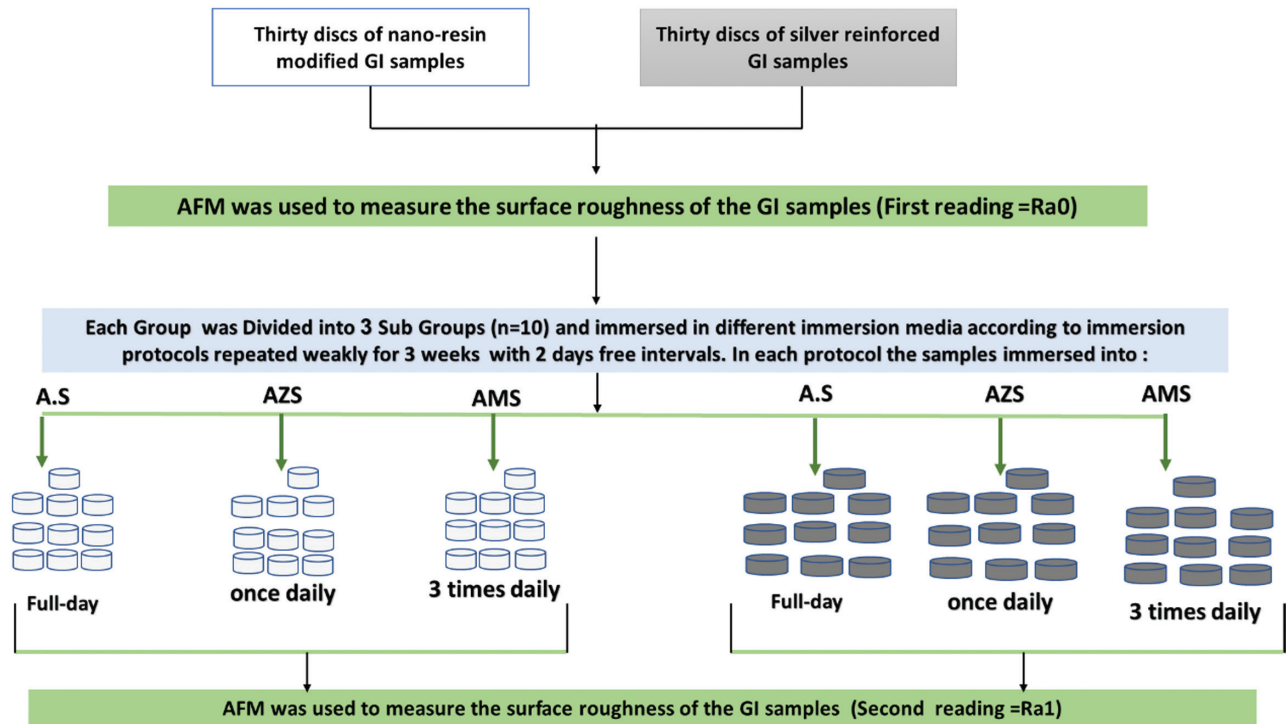


Figure 1: A flowchart of sample distribution and measured parameter

0.01 g, and one gram of sodium chloride, sorbitol and potassium chloride.^[21]

Deionized water (900ml) was used to dissolve all of the above substances. After that, boiling water (100 ml) was required to dissolve sodium carboxymethyl cellulose (10g) and then the solution was left to cool down before its addition to the previous ingredients. After that, the pH of artificial saliva was modulated to 7. A professional benchtop pH meter consisting of a glass electrode and an electronic meter was used for measurements of pH in this study. The glass electrode was firstly calibrated using buffering solutions with known pH level solutions (4.0, 7.0, 9.0).^[21]

Two commercial antibiotics were used in this study, the AZi-Once and amoxicillin BP suspensions. Azi-Once (Jamjoom Pharmaceuticals Co., Saudi Arabia, MWT 748508) consists of: Azithromycin oral suspension 200mg/5mL with excipients include: banana flavor, colloidal silicon dioxide, fantasy flavor permaseal, fresh co forte permaseal, hydroxypropyl cellulose, sucrose trisodium phosphate monohydrate, xanthan gum and purified water. Amoxicillin BP sugar-free suspension (Athlon Laboratories, Ireland, MWT 419.4) consists of: Amoxicillin oral suspension 250mg/5mL, sorbitol solution BP, sodium benzoate, disodium edetate, sodium citrate, orange bramble flavor, quinoline yellow, citric acid, colloidal anhydrous silica, xanthan gum, sorbitol and saccharin sodium.

To conduct pH measurements of antibiotic suspension, the glass electrode of the pH meter was separately immersed into a glass beaker containing 20 mL of each antibiotic suspension at room temperature (25°C). To avoid any potential cross-contamination, the glass electrode of the pH meter was carefully dried with cotton pads after being washed with distilled water before each pH measurement. The recorded pH values were 4.1 for AMS (representing the acidic media), and 9.2 for AZS (representing the basic media). To ensure the precise readings of pH, the pH values of each antibiotic suspension represented a mean of three readings.

IMMERSION PROTOCOLS

Immersion cycles were performed by separately immersing the GI discs in the immersion media over a period of 25 days (7 days for three consecutive immersion protocols at 2-day intervals) in accordance with the following sessions: AMS for 2 minutes three times daily and AZS once daily. After every sample immersion period, the GI discs were rinsed and kept in A.S up to the next immersion time. Control samples were kept in A.S, which was refreshed daily. SR was evaluated twice: before the first immersion cycle (baseline or R0) and after the third immersion cycle.

SURFACE ROUGHNESS ASSESSMENT

Atomic force microscopy (AFM, Naio AFM 2022, Nanosurf AG, Switzerland, version 3.10.0)

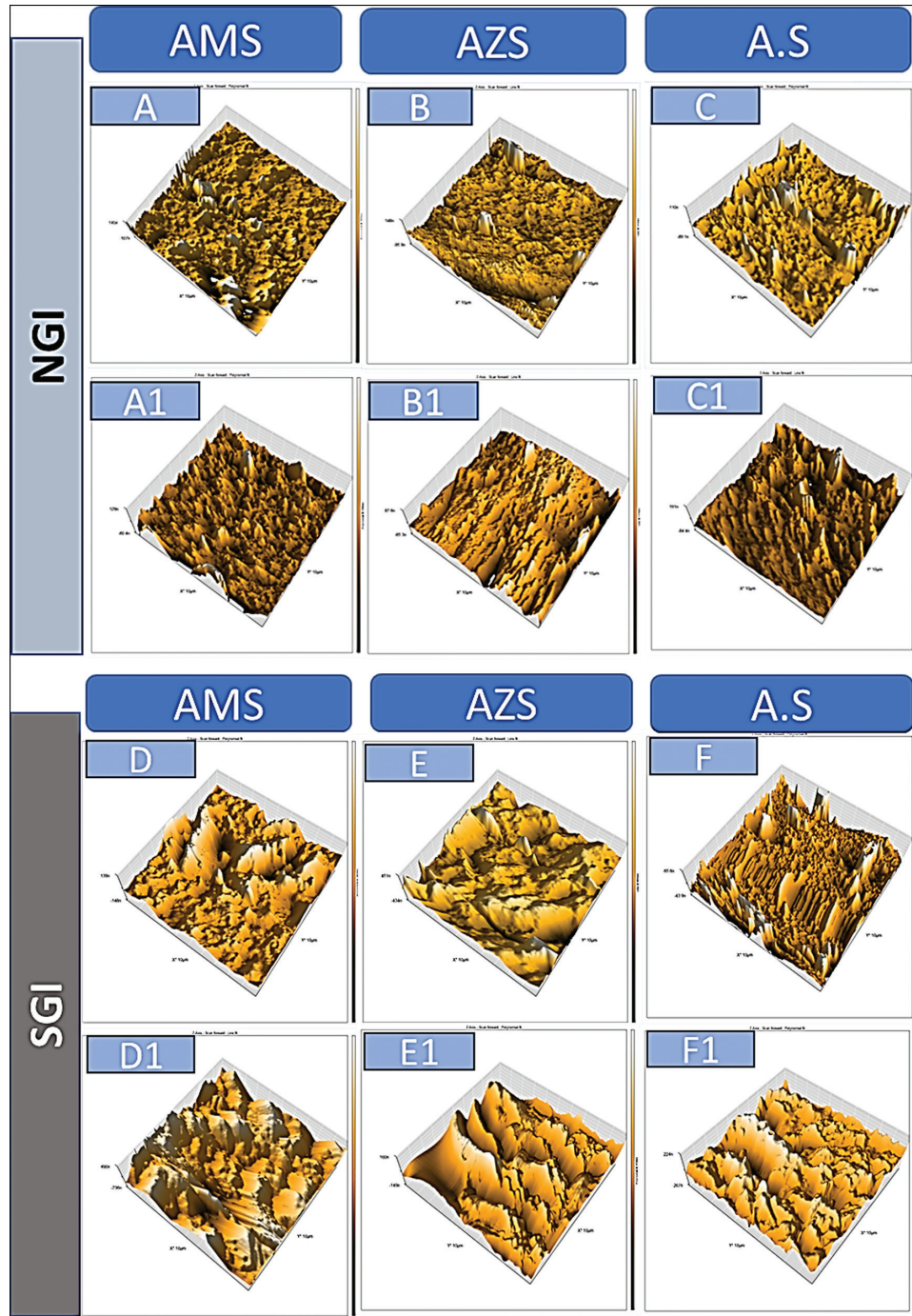


Figure 2: 3D AFM topography of NGI and SGI samples. (A), (B) and (C) represent NGI samples, while (D), (E), and (F) represent SGI samples before immersion in AMS, AZS, and AS, respectively. (A1), (B1), and (C1) refer to the NGI samples, while (D1), (E1), and (F1) refer to the SGI samples, following the third immersion cycle

was utilized to evaluate the SR of the GI samples initially (Ra0) and after day 25 (Ra1). Scanning was performed using a tapping mode on $10\ \mu\text{m} \times 10\ \mu\text{m}$ areas at 1 Hz scanning speed with a scan at its center.^[20] Roughness was measured in nanometers to quantify surface texture and measured using Ra parameters (the arithmetic mean of the peak height and valley depth from the mean line), which depict the total SR

of a sample.^[21-23] AFM 3D images were acquired at a resolution of 1024×1204 pixels.

STATISTICAL ANALYSIS

Statistical analysis was carried out on SPSS version 22. Description statistics were represented by the mean and standard deviation. Paired *t* test and independent *t* test were used for intra- and inter-group comparisons at a significant

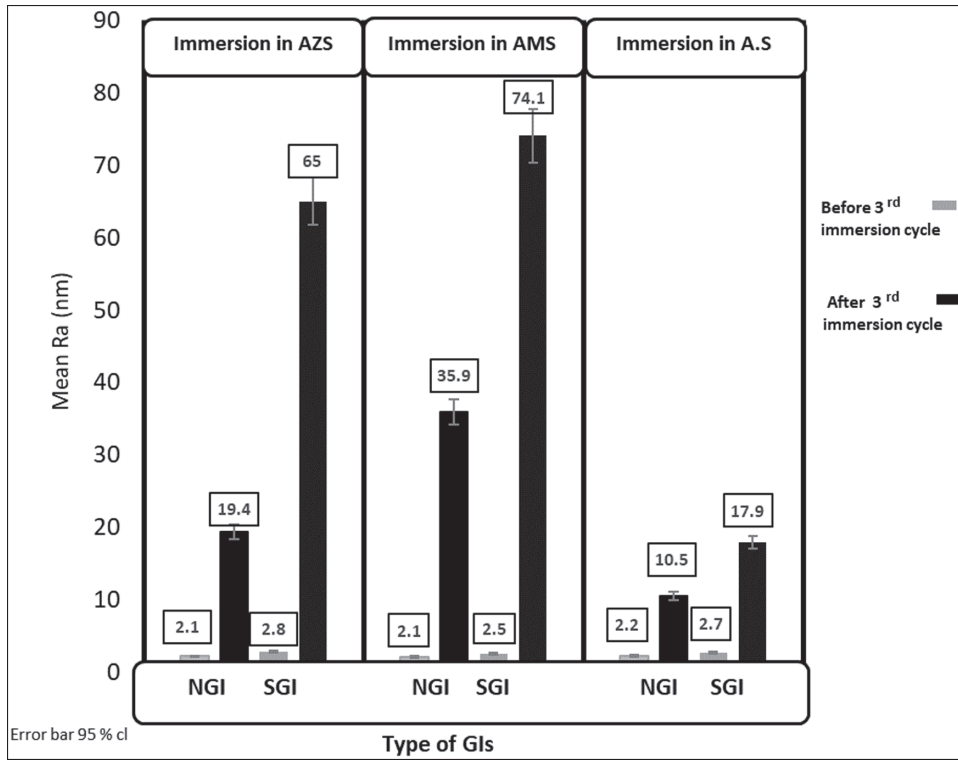


Figure 3: Mean values of SR measurements (Ra) of the GI samples before and after immersion cycles. NGI represents the nano resin-modified glass ionomer, while the SGI represents the SGI

Table 2: Statistical comparisons of the SR values of restorative materials before and after immersion in different media

Immersion media	Ra0 mean ± SD (nm)			Ra1 mean ± SD (nm)		
	Nano resin-modified glass ionomer	SGI	P value	Nano resin-modified glass ionomer	SGI	P value
AZS	2.2 ± 1.2 Aa	2.7 ± 1.2 Aa	0.11	19.3 ± 3.9 Ba	65.0 ± 6.3 Ba	<0.001*
AMS	2.1 ± 0.5 Aa	2.5 ± 0.3 Aa	0.23	35.9 ± 6.6 Bb	74.1 ± 10.1 Bb	<0.001*
AS	2.2 ± 0.7 Aa	2.7 ± 0.6 Aa	0.12	10.5 ± 0.2 BC	17.9 ± 2.8 BC	<0.001*
ANOVA	F	0.04	0.34	48.2	263.3	
	P value	1.0	0.7	<0.001*	<0.001*	

Dissimilar capital letters indicated intra-group statistics. Significant differences between baseline and post-immersion readings (horizontal line)

Dissimilar small letters indicated intra-group statistics. Significant differences between baseline and post-immersion readings (vertical line)

*Indicates statistically significant difference between the two groups (nano resin-modified GI vs. SGI) for the base line and post-immersion readings independently

level of $P < 0.05$. Two-way repeated measure analysis of variance (ANOVA) was utilized to study the SR changes in the GIs between the immersion media. The Bonferroni *post-hoc* test was applied to determine the significant differences between groups at a significant level of $P < 0.05$.

RESULTS

1. **pH measurements:** The recorded pH of AZS was 9.2 (basic medium). The acidic medium was AMS with a pH of 4.1. The AS was a neutral medium with a pH of 7.0.

2. AFM topography and SR analysis:

a. **AFM topography:** The AFM topography demonstrated the comparisons of SR between NGI and SGI samples before and after immersion in different media. Initially, the SR of these GIs exhibited differences in filler shape and size. The SGI samples had a higher number of peaks and valleys and prominent protrusions than the NGI samples, creating a more heterogeneous appearance for the former. These findings were numerically supported by

the SGI samples exhibiting higher Ra values than the NGI sample [Figure 2].

A normality test was conducted on the surface roughness data using Shapiro Wilk test with a significance level set at $p < 0.05$. This test illustrated that the data were normally distributed across various parameters, involving interval of time measurements, kinds of GI, and the immersive media that were used.

Considering the difference in GI type, SGI showed higher SR values before and after immersion in liquid medications than NGI [Figure 3].

Table 2 illustrates the average SR values of the GIs before and after immersion cycles in different media and the intra-group pairwise comparison results. The intragroup comparisons of the SR of each GI type demonstrated significant differences when analogized before and after the immersion cycles ($p < 0.05$). ANOVA revealed that the intragroup comparisons of the SR of the GIs samples before immersion cycles did not significantly differ ($p > 0.05$), whereas significant changes in the SR were illustrated after immersion in AZS, AMS, and A.S ($p < 0.05$). Besides, the AMS suspension massively roughened the surface of the GIs and demonstrated higher variations in the SR values of GI samples than the AZS and A.S [Table 2]. The latter demonstrated the lowest roughened effect as minimal changes in the Ra values were observed in the GI samples. A multiple pairwise comparison test (Bonferroni post-hoc test) was used to specify the significance of different immersion media on the SR of GIs. The results revealed that all the three-immersion media exhibited significant roughened ($p < 0.05$) in the SR of NGI and SGI when compared with one another. Meanwhile, the intergroup comparisons demonstrated no significant differences ($p > 0.05$) when the initial SR values (Ra0) of the NGI samples were compared with those of the SGI samples. However, significant differences were reported between the Ra1 values of the NGI and SGI samples after separate immersion in AZS, AMS, and A.S ($p < 0.05$).

DISCUSSION

Considering the use of GIs and liquid antibiotics may be unavoidable during childhood.^[24] The present research was designed to assess the detrimental impacts, if any, on the SR of GIs induced by AZS and AMS antibiotic suspensions that are frequently used to treat pediatric bacterial infections. The main focus was on roughness changes, because SR plays a crucial role in retaining the intraoral microorganisms, and it induces swifter colonization.^[25] So, an increase in SR could increase the

likelihood of dental cavities and periodontal infections.^[25] Accordingly, a smoother surface of restorative materials could reduce the ability of surface bacterial attachment, reduce bacterial colonization, and subsequently prevent biofilm formation.^[25] SR was evaluated using AFM because it provides high-resolution images, 3D imaging, and overall information about surface heterogeneity and particle distribution.^[26] NGI exhibited lower SR value and more resistance to environmental changes than SGI, which may be due to the nature of NGI's physical characteristics in comparison to that of SGI. These differences can be assigned to the shape, number, and distribution of the particles and the differences in interfacial bonding between particles.^[27] Incorporating nano-filler particles can fill up the spaces between GI particles, leading to improvement in GI composition, thereby reinforcing the material and supporting higher micro-mechanical interlocking that could enhance the chemical energy stored in the covalent bond of NGI. Hence, the addition of nano-filler particles could render NGI more resistant to environmental changes with a smoother surface than other types of GI cements.^[9,25] Meanwhile, the SGI structure was more porous than the NGI structure, leading to increased porosity that can increase water absorption and uptake through polymer chains. This process could modify and decrease the physical and mechanical features of restoration because the loss of chemical bond between filler particles, which ultimately may cause increased SR.^[28] Higher SR changes were obtained in acidic media (AMS) compared to basic and neutral ones, mainly due to their abrasive and erosive nature. This detrimental effect can be attributed to the dissolution of particles in the surface of the restorative materials, inducing a rise in the SR values of GI.^[29]

Many studies approved the negative outcome of low pH media on the restorative materials and came in a line with what was found in the present study.^[1,29-31] For example, De Paula *et al.* (2014) showed that the degradation of nano-filler GIs by orange juice and Coca-Cola caused a significant increase in SR.^[30] In an interesting study conducted by Perera *et al.* (2020), the acidic materials used (citric acid, phosphoric acid and lactic acid) exhibited significant destructive impacts on different types of GIs, after 14-day immersion period distinguishing the citric acid as the most erosive material.^[32] Daily consumption of acidic beverages can exacerbate the influence of acidic materials on the SR of GIs as demonstrated by Colombo *et al.* (2021), who attributed this finding to the solubilizing effect of the acidic media.^[29] More aggressive conditions were applied by Tărăboanță *et al.* (2022) who exposed the resin-modified

glass-ionomer cements to gastric juice with brushing effect for 30 min post the acidic attack for one year, and found a significant increment in SR of the tested materials.^[33] In addition to the current study, all the abovementioned studies adopted the same concept in explaining the main cause behind the acidic effect on the SR of the restorative materials, specifically the GIs, which can be underpinned by the hydrolysis of the GI surfaces. As the restorative materials are considered as ion releasing materials,^[33-35] the detrimental effect of the low pH solutions on the SR of the GIs can be traced back to the aggressive attack and exchange of the surface ions with the H⁺ ions of the acidic media.^[36] In addition to the ability of acidic materials to strongly chelate with the surface ions leading to a marked dissolution and increment in surface roughness.^[36] Zaki *et al.* (2012) also mentioned that after immersing the GI in an acidic media, the solution infiltrates inside the cement and expands the gel matrix.^[37] Furthermore, diffusion of the hydrogen ions (H⁺) into the matrix inducing changes in metal cations, which disseminate into the solution when the concentration gradient decreases.^[36-39] As a result of the metal cations dissemination, the free oxygen concentration increases, leading to dissolution of the GI surface and an increase in its surface roughness.^[36,40,41]

CONCLUSION

AMS, AZS, and AS (acid, alkaline, and natural pH media, respectively) significantly altered and increased the SR of both NGI and SGI. However, NGI exhibited smoother surfaces and higher resistance to alterations caused by oral liquid medications, particularly AMS (acidic medium), compared to SGI. Notably, this study is the first to report that alkaline drugs (AZS) could significantly impact the SR of GIs. Parents are strongly recommended to be educated and advised to brush their child's teeth or at least teach them to use the "swish and spit" method after consumption of pediatric liquid medications. This practice could help avoid the harmful effects of these drugs on restorative materials. Due to the limitations of an *in vitro* study, clinical studies should be conducted to evaluate the intraoral durability of SGIs and NGIs.

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Nil.

CONFLICTS OF INTEREST

There are no conflicts of interest.

AUTHORS CONTRIBUTIONS

ZH, NA study conception and design. ZH data collection. ZH, NA Methodology. ZH, NA and AI statistical analysis and interpretation of results. ZH, NA and AI original draft manuscript preparation. ZH, NA and AI writing - review & editing. Supervision NA; All authors reviewed the results and approved the final version of the manuscript to be published.

ETHICAL POLICY AND INSTITUTIONAL REVIEW BOARD STATEMENT

The Research Ethical Committee at the University of Baghdad College of Dentistry, Department of Basic Sciences, has reviewed the submitted research project outline below for ethical approval on February 6, 2022, Reference No. 573.

PATIENT DECLARATION OF CONSENT

Not available.

DATA AVAILABILITY STATEMENT

Not available.

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