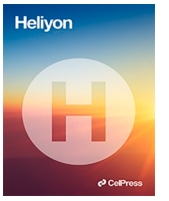
Heliyon 10 (2024) e35189

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

Enhancing orthopedic outcomes: A comparative analysis of gentamicin sulphate and nanosilver in bone cement

Aysu Aydınoğlu

Yıldız Technical University, Faculty of Chemistry and Metallurgy, Department of Metallurgy and Materials Engineering, Istanbul, 34349, Turkiye

A B S T R A C T

Background: Orthopedic surgeries frequently utilize bone cement, which can increase the risk of postoperative infections. Addressing this challenge, this study aims to enhance the mechanical, physical, and handling properties of bone cement by integrating gentamicin sulfate (GS) and nanosilver (nAg). The objective is to evaluate and compare the effects of these additives on properties such as compressive strength, flexural strength, doughing time, working time, setting time, and exothermic temperature. By doing so, the study seeks to identify a safer and more effective alternative to traditional antibiotics in bone cement formulations, thereby improving clinical outcomes in orthopedic procedures.

Methods: This research involved a comparative analysis of modified cements against standard cements, focusing on compressive strength, flexural strength, doughing time, working time, setting time, and exothermic temperature. Various bone cement samples with GS and nAg additives were prepared and tested in accordance with international standards (ISO 5833:2002 and ASTM F451). Statistical analysis, including one-way and two-way ANOVA tests, was used to assess the significance of the results.

Results: nAg-loaded cements exhibit mechanical and physical properties on par with or supe-rior to those of GS-loaded and standard cements. Notably, nAg incorporation leads to significantly lower exothermic temperatures, reducing the risk of thermal bone tissue damage. This finding highlights that nAg-loaded cement is a safer alternative. Alongside unaltered or enhanced strength, nAgs demonstrate promise for orthopedic applications, particularly in primary arthroplasty. Additionally, nAgs reduce doughing time, enhancing the practicality of these methods in surgical settings.

Conclusions: In conclusion, this study underscores the potential advantages of incorporating GSs and nAgs into bone cement. nAg-loaded cement offers improved properties and reduced infection risk, making it a valuable choice for orthopedic procedures. It enhances both mechanical performance and safety, addressing crucial concerns in orthopedic surgery.

1. Introduction

Orthopedic procedures, particularly joint replacements such as hip and knee arthroplasty, have become increasingly common, presenting significant challenges to both the medical and scientific communities [1]. One of the major complications associated with these surgeries is the potential for postoperative infections, which can lead to prolonged hospital stays, increased financial burdens, and substantial morbidity [2].

Bone cement, primarily composed of polymethyl methacrylate (PMMA), plays a crucial role in these surgeries by stabilizing prosthetic implants [3]. Enhancing the antimicrobial properties of this cement is a viable strategy to reduce infection rates [4–7]. Various antibiotics, including levofloxacin [8], gentamicin [9], vancomycin, and tobramycin [10], have been tested for their efficacy when added to bone cement. Among these, gentamicin sulfate (GS) has garnered substantial attention due to its prolonged antibiotic release compared to other antibiotics [11]. However, the rise of bacterial resistance to common antibiotics necessitates the exploration of alternative antimicrobial agents [9].

Nanometallic materials such as nano silver (nAg) [12–14], nano gold (nAu) [10], nano titanium (nTi) [15], nano copper (nCu) [16]

E-mail address: aysuaydn@yildiz.edu.tr.

https://doi.org/10.1016/j.heliyon.2024.e35189
Received 6 March 2024; Received in revised form 18 July 2024; Accepted 24 July 2024
Available online 25 July 2024
2405-8440/© 2024 The Author. Published by Elsevier Ltd. This is an open access article under the CC BY-NC license (http://creativecommons.org/licenses/by-nc/4.0/).

and nano zinc (nZn) [17], are known for their superior antibacterial properties and wide range of applications Among those, nAg has been the most extensively studied due to its well-documented ability to combat infections [18]. Several studies have demonstrated the bactericidal efficacy of nanosilver in bone cement, particularly against multidrug-resistant bacteria. However, these studies often do not thoroughly examine the mechanical, physical, and handling properties of bone cement with added nanometals [4,19–26].

For instance, Swieczko-Zurek et al. [16] various nanometals, including silver and copper, in terms of their biological properties and compressive strength. Both nAg and nCu are renowned for their antibacterial effects, but their influences on the overall features of bone cement, including its mechanical, physical, and chemical properties, have yet to be comprehensively investigated. Compared to other research, this presented study emphasizes the handling properties of bone cement, such as doughing time, working time, setting time, and exothermic temperature, which are crucial for practical surgical applications and have been less emphasized in previous studies.

The long-term stability of acrylic bone cement is closely related to its mechanical properties. According to ISO 5833 and ASTM F451 standards, bone cements must have a bending strength of over 50 MPa, a bending modulus exceeding 1800 MPa, and a compressive strength above 70 MPa [27,28]. Maintaining the correct powder/liquid (P/L) ratio in bone cement formulations is critically important, as deviations can significantly impact mechanical properties [29]. Additionally, even small amounts of blood contamination can substantially weaken bone cement's mechanical properties, leading to flexural and compressive strengths that fall below required standards [30]. Recent studies have also examined the effects of aggressive environments, such as Ringer's solution, on bone cement, revealing that these factors can decrease compressive strength [31].

Advancements in bone cement formulations have included the incorporation of various additives to enhance properties. Nanoparticles such as magnesium oxide (MgO) and titanium dioxide (TiO_2) have shown promise in improving the mechanical strength, biocompatibility, and overall performance of bone cement [32].

[27,28]In cemented joint arthroplasty, the handling properties of acrylic bone cement play a crucial role in determining the duration of the operation. The polymerization process of acrylic bone cement includes four stages: mixing, doughing, working, and setting. The doughing time, which is the time required for the cement mixture to reach a homogeneous dough-like state, is critical for surgical applications [33]. The doughing time is related to the dough viscosity [34] as well as the interactions between the dough and additives [35]. The setting time, the duration until the cement is completely cured after mixing, is another important criterion [36]. The interval between doughing time and setting time is referred to as the working time [27].

Orthopedic acrylic cements must also manage the exothermic polymerization reaction to prevent thermal necrosis of the bone tissue [37]. In this respect, containing the maximum exothermic temperature is paramount for preventing thermal necrosis of the bone tissue while the cement sets. Basically, the more heat the BC generates during polymerization, the more harmful it is to the surrounding bone tissue [38]. The maximum temperature attained during the hardening of BC should not exceed 90 ± 5 °C. Furthermore, one of the factors to be considered when choosing antibiotics is the ability to withstand exothermic heat. Indeed, many antibiotics, such as erythromycin, colistin, gentamicin, and tobramycin, are used in bone cement applications because of their heat resistance [39,40]. The polymerization temperature of MMA can reach 100 °C. A common way of preventing such dangerous heat release is to fix polymer/monomer ratios to 2/1 (w/w) [41]. Another useful option is to use nanoparticles such as nAgs, which can suppress exothermic reactions in bone cement due to their greater surface area. Additionally, silver possesses only two oxidation states (0, +1), implying that a reduction involving Ag^0 would probably involve a single-electron transfer. In fact, neither Ag0 nor its oxidized form, Ag^{+1}, are soluble in most reaction media. Finally, Ag^0 is largely unreactive to standard polymerization agents, which might reduce or even prevent the unwanted radical formation or termination events often observed in atom transfer radical polymerization (ATRP) methods [42].

The purpose of this study is to address critical clinical challenges such as infection control and antibiotic resistance in orthopedic surgeries. While gentamicin is effective, it is associated with increasing antibiotic resistance, necessitating the search for alternatives. Nanosilver (nAg) has been proposed as a promising alternative due to its superior antibacterial properties. However, most studies to date have primarily focused on its antimicrobial effects, with limited investigation into other crucial properties such as handling, setting time, exothermic temperature, and mechanical strength. This study aims to demonstrate the enhanced properties and reduced thermal damage associated with nanosilver-loaded cement, highlighting its significant clinical potential as a safer and more effective alternative to traditional antibiotics in bone cement formulations. By demonstrating the enhanced properties and reduced thermal damage associated with nAg-loaded cement, this study not only underscores the antibacterial potential of nanosilver but also provides comprehensive insights into its handling and mechanical performance [27,28].

2. Materials and methods

2.1. Material preparation

A commercially available low-viscosity PMMA bone cement, Betacem LV (Turkey), was obtained from Betatech Medical. The powder component of the cement comprises poly(methyl methacrylate), barium sulfate, and benzoyl peroxide, while the liquid primarily contains methyl methacrylate supplemented with minor quantities of N,N-dimethyl-p-toluidine and hydroquinone.

Experimental bone cements were formulated by blending various antimicrobial additives with the powdered form of commercial acrylic bone cement. As antimicrobial agents, gentamycin sulfate (GS; Pharma grade, CAS-No. 1405-41-0; Sigma–Aldrich; purchased from Kimetsan, Turkey) and nanosilver (nAg; 20 nm, 100 % purity; CAS-No. 7440-22-4; US Research Nanomaterials, Inc., purchased from Nanokar, Turkey) were incorporated in PMMA powder in a proportion of 4 g (GS-PMMA sample) and 2 g (Ag-PMMA sample), respectively. Antibiotics were loaded manually according to the manufacturer's recommendations [43]. Commercial

polymethylmethacrylate cement, referred to as the PMMA sample, was utilized for comparison. Table 1 below displays the chemical compositions of both the reference commercial cement and the newly developed experimental bone cements. The liquid component was combined with the premixed powders at a liquid-to-solid ratio of 1:2. This mixture was agitated for 2 min. Once the plants ceased adhering to the gloves, they were then poured into molds, which were sized appropriately for subsequent analysis (Fig. 1). All the materials, equipment, and mixing surfaces were maintained at 23 ± 1 °C prior to and during testing.

2.2. Mechanical characterization

Both the control group and the loaded experimental bone cement group underwent compression and four-point bending tests. Five samples for each formulation (PMMA-BC, GS-BC, and Ag-BC) were prepared in a cylindrical mold for the compression test (6 mm diameter and 12 mm height). Five samples from each formulation (PMMA-BC, GS-BC, and Ag-BC) were placed in a cylindrical mold measuring 6 mm in diameter and 12 mm in height for the compression test. Once cured, each sample was removed from the mold and smoothed using SiC abrasive paper to remove all superficial roughness. The examination was conducted in accordance with ISO-5833 (2002) Annex-E, titled "Determination of Compressive Strength of Polymerized Cement" [27], using a Devo-trans universal testing machine with a cross-head speed of 20 mm/min. The upper yield-point load was used to calculate the compressive strength via Equation (1). All the presented data are expressed in terms of means and standard deviations. The results were evaluated using ANOVA, and a p value of less than 0.05 was considered to indicate statistical significance.

$$CS = F/A \tag{1}$$

where F is the upper yield-point load (N), A is the specimen cross-sectional area (mm^2), and CS is the compressive strength (MPa).

Similar protocols to those used for the compression test were applied to conduct the bending test. Five bar samples (75 × 10 × 3.3 mm) of PMMA, GS-BC, and Ag-BC were prepared to determine the 4-point bending strength and bending modulus in accordance with ISO-5833-2002, annex F [27]. The samples were shaped in a rectangular mold, and upon curing, they were refined using 600-grit SiC abrasive paper to achieve the desired dimensions. Like in the compression test, all the presented data are expressed as the means and standard deviations. The universal test machine (Instron) had a cross-head speed of 5 mm/min and was equipped to measure and record the deflection of the specimen's center. The force applied to the central loading points began from zero and escalated until the specimen fractured. The flexural modulus and flexural strength of each test specimen were determined using Equation (2) and Equation (3), respectively. The results were assessed using ANOVA, and a p value less than 0.05 was considered to indicate statistical significance.

$$E = \Delta Fa\,/\,(4fbh\hat{3}) \times (3\,\hat{l}2 - 4\hat{a}2) \tag{2}$$

where f is the difference between deflections under loads of 15 N and 50 N (mm), b is the average width of the specimen (mm), h is the average thickness of the specimen (mm), l is the distance between outer loading points (60 mm), ΔF is the load range (50 N–15 N = 35 N), a is the distance between the inner and outer loading points (20 mm), and E is the flexural modulus (MPa).

$$B = 3Fa/(bh\hat{2}) \tag{3}$$

2.3. Handling properties (Dowing time, setting time, working time) and exothermic temperature

The doughing time, setting time, working time and exothermic temperature of the bone cement were assessed in accordance with ISO 5833–2002, and three tests were conducted (n = 3) for each parameter. The bone cement powder was transferred to a plastic bowl for mixing. After 20 ml of liquid monomer contacted the powder, a stopwatch was applied. The ingredients were mixed manually using a spatula. After 1 min, the paste was gently mixed using a powder-free latex-gloved finger. If a fibrous connection formed between the glove and the cement when the finger was removed, the touch test was repeated at 15-s intervals. The point at which the glove could be lifted without any residue remaining was noted as the cement's "dough time". For each test, a fresh section of the glove was utilized, ensuring that the cement was lightly stirred before touching.

To measure the exothermic temperature, powders were mechanically mixed with liquid MMA. After mixing, the mixture was placed in a mold equipped with a thermocouple in accordance with ISO 5833 requirements. The temperature increase was logged every 1 s. Based on the collected data, the exothermic temperature (T_{max}), the setting temperature (T_{set}), and the setting time (t_{set}) were

Table 1
Composition of the control group and experimental bone cements.

Samples	Composition		Antimicrobial Additive
	Powder	Liquid	
PMMA-BC (control)	PMMA, BPO, $BaSO_4$	MMA, DMPTT, HQ	None
GS-BC	PMMA, BPO, $BaSO_4$	MMA, DMPTT, HQ	2 g gentamicin sulfate (GS) was incorporated in powder
Ag-BC	PMMA, BPO, $BaSO_4$	MMA, DMPTT, HQ	2 g nano silver (nAg) was incorporated in powder

Methyl methacrylate—MMA; N,N-Dimethyl-p-toluidine—DMPT; Hydroquinone—HQ; Poly(methyl-methacrylate)—PMMA, Benzoyl peroxide—BPO, Barium sulfate—$BaSO_4$

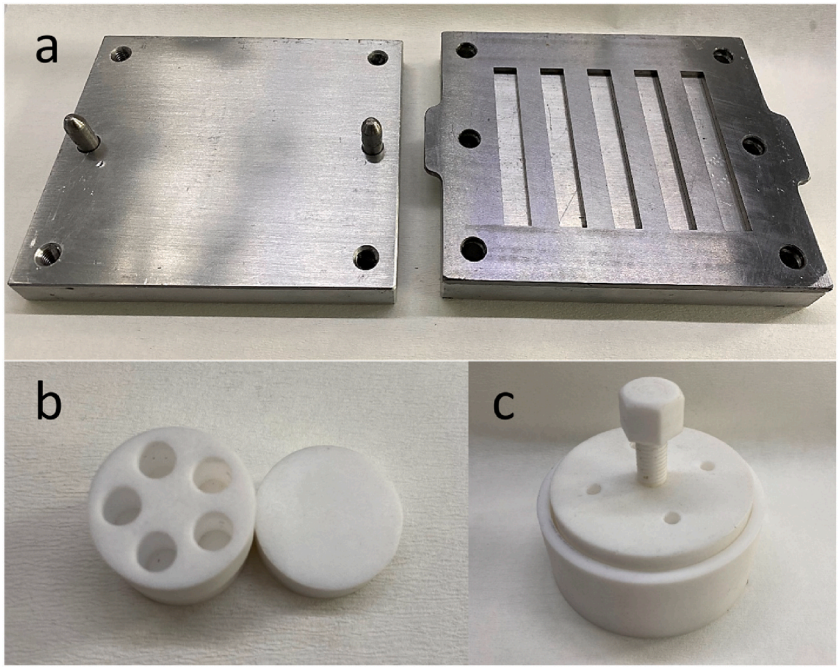


Fig. 1. Molds used to form specimens. All the molds were designed according to ISO 5833:2002: a) The mold for the 4-point bending test, b) The mold for the compression test, and c) The mold for the exothermic temperature.

determined. The setting time was defined as the time required for the mixture to reach the midway temperature between the ambient temperature and the maximum temperature. The setting temperature (T_{set}) was calculated using Equation (4), and this temperature was recorded as the settling time (t_{set}). The working time was calculated as the difference between the setting time and the doughing time.

$$T_{set} = (T_{max} + T_{amb})/2 \quad (4)$$

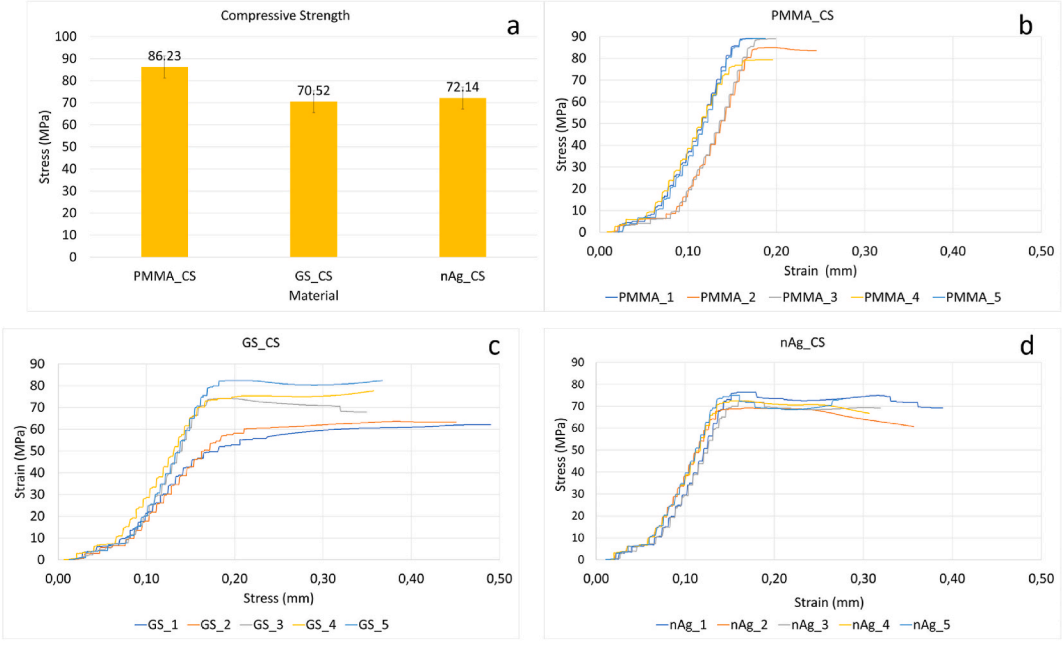


Fig. 2. The compressive strength of the bone cements was assessed following the ISO 5833-2002 standard. (a) Intergroup comparisons; (b) An example of a sample stress–strain curve for each specimen.

where T_{amb}: ambient temperature (°C) and T_{max}: highest temperature recorded (°C). T_{set}: Setting temperature (°C).

2.4. Statistical analysis

All descriptive data are presented as the arithmetic mean and standard deviation. Differences among the three types of bone cement were examined using one-way analysis of variance (ANOVA). At multiple time points, two-way ANOVA was used to analyze the differences among the three bone cement types. A p value of less than 0.05 was considered to indicate statistical significance for all tests. The statistical evaluations were performed using SPSS software (version 27.0; IBM, Inc., Armonk, NY, USA).

3. Results

3.1. Mechanical characterization

Fig. 2 presents the outcomes of the compressive strength assessment following the ISO 5833-2002 standards [44]. The average compressive strength values are depicted in Fig. 2a, while Fig. 2b–d displays representative stress–strain curves for each sample type. Notably, no significant variation was observed between the GS and nAg additions ($p = 0.423$). Conversely, the compressive strength (CS) values of the PMMA bone cement significantly decreased upon the inclusion of both GS ($p = 0.006$) and nAg ($p = 0.004$). Nonetheless, from a compression perspective, the compressive strengths of all the composite samples met the ISO standard minimum threshold of 70 MPa.

To further investigate the mechanical characteristics of the composites, the bending strength was assessed in accordance with the ISO-5833 standard [44]. Fig. 3 displays the bending strength and bending modulus data. PMMA, GS-loaded, and nAg-loaded bone cement achieved the required bending strength per ISO standards (50 MPa) (Fig. 3a). Although the addition of nAg led to a reduction in bending strength, the differences among the various formulations lack statistical significance according to Student's *t*-test ($p = 0.676$). With regard to the bending modulus, all the attained values exceeded the ISO standard threshold (1800 MPa, $p = 0.247$) (Fig. 3b).

3.2. Doughing time, setting time, working time and exothermic temperature

Table 2 shows the results of the dough time determination. The drying time should be $\leq 5 \pm 1.5$ min according to ISO 5833:2002 [44]. Therefore, all the groups met the minimum requirements of the standard. However, the addition of nAg significantly decreased the doughing time of PMMA and GS-loaded bone cement ($p = 0.000$). On the other hand, there were no significant differences between the doughing times of PMMA and GS-loaded bone cements ($p = 0.994$).

Fig. 4 illustrates the temperature progression for each cement formulation as acquired from the setting time assessment. Additionally, Table 2 presents the mean values for setting time (t_{set}) and setting temperature (T_{set}), along with the highest recorded exothermic temperature (T_{max}) and polymerization time (t_{max}). The exothermic (T_{ex}) and setting (T_{set}) temperatures of the bone cements were significantly different between the two groups ($p < 0.05$). nAg loading significantly decreased the T_{max} ($p = 0.000$) and T_{set} ($p = 0.000$), while GS addition increased Tex ($p = 0.010$) and T_{set} ($p = 0.001$). Moreover, compared to those following GS incorporation, the addition of nAg also significantly decreased the T_{ex} ($p = 0.000$) and T_{set} ($p = 0.000$) levels. The setting time and working time of the bone cements were significantly different ($p = 0.000$). In that manner, GS-loaded cements have the highest setting and working times, while PMMA cements have the lowest setting and working times. Nonetheless, the parameters obtained are in line with ISO stipulations, adhering to the range of 3–15 min for setting time (t_{set}) and a maximum temperature (T_{max}) of 90 °C [44]. Concerning polymerization time (t_P), there was no significant difference among the $_{tP}$s for PMMA and nAg-loaded bone cements ($p = 0.242$). However, GS addition significantly increased the polymerization time compared to that of PMMA ($p = 0.007$) and nAg-loaded ($p = 0.001$) cements.

4. Discussion

This study addressed a question of both clinical and scientific significance: does the addition of nanosilver (nAg) present distinct advantages compared to those of gentamicin sulfate (GS)-loaded bone cements? The investigation involved a composite bone cement comprising a PMMA matrix combined with gentamicin sulfate and nanosilver. To further explore this phenomenon, a low-viscosity

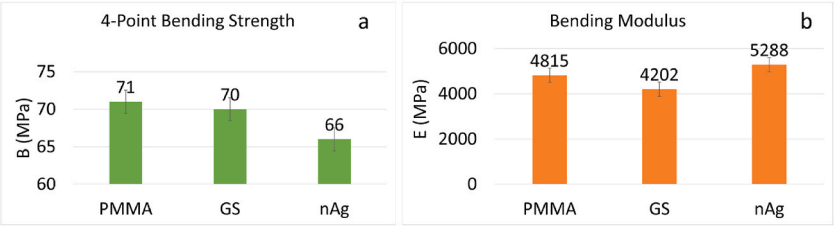


Fig. 3. (a) 4-point flexural strength and (b) bending modulus evaluation of the PMMA, GS-loaded and nAg-loaded bone cements.

Table 2
Dough time, setting time, working time and exothermic temperatures of PMMA, GS-loaded and nAg-loaded bone cements.

	PMMA_BC	GS_BC	nAg_BC
Doughing Time (min)	3.30 (±0.02)	3.31 (±0.11)	2.51 (±0.0.02)
Setting Time (min)	9.50 (±0.03)	11.40 (±0.16)	9.55 (±0.08)
Setting Temperature (°C)	49.07(±0.50)	51.53 (±0.29)	42.70 (±0.29)
Working Time (min)	6.20 (±0.05)	8.09 (±0.06)	7.04 (±0.10)
Exothermic Temperature (°C)	74.3 (±2.2)	80.8 (±0.82)	61.37 (±0.78)
Polymerization time (min)	11.24 (±0.08)	12.63 (±0.37)	10.72 (±0.32)

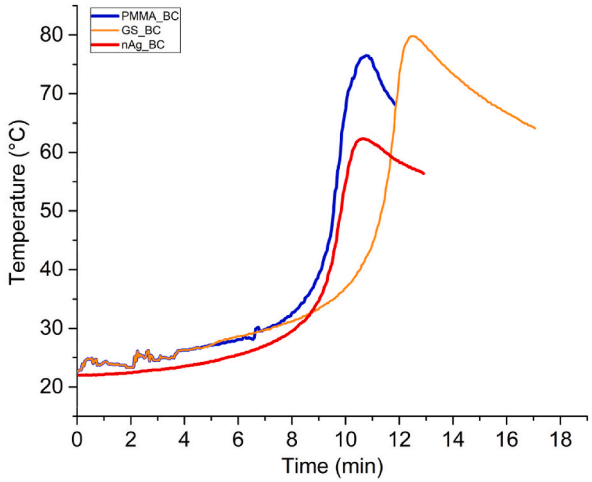


Fig. 4. Setting time and exothermic temperature evaluation of the bone cements.

commercial bone cement served as the polymeric matrix, and the present research specifically investigated how the incorporation of GS and nAg influenced the physical and mechanical attributes of the composite cement.

The fundamental functions of bone cement include ensuring immediate implant fixation postsurgery and distributing loads from the implant to the adjacent bone bed to prevent stress shielding. Consequently, it is imperative that any additives introduced to cement do not significantly alter its intrinsic mechanical characteristics. All three bone cement types tested in this study met the standard mechanical property requirements, especially for flexural strength and modulus (Fig. 3). The compressive strength test revealed no statistically significant difference between the control (PPMA) and nAg-loaded groups but that the nAg significantly improved with increasing GS loading. This enhancement can be attributed to a more consistent dispersion within the PMMA matrix, allowing nAg to effectively distribute stress across the matrix. As a result, there are no evident "macroscopic" weak links present within it [45]. Furthermore, polar interactions are more likely to occur between the C=O groups of the PMMA chains and nAg. This enhances the compatibility between the polymeric matrix and the nanoparticles [46]. However, the compressive strength significantly decreased with the addition of GS ($p < 0.01$), which is in line with the findings of prior literature [47]. Flexural properties, on the other hand, were not significantly affected by the addition of nAg or GS, as shown in Fig. 3. Specifically, the flexural modulus was not affected by the incorporation of GS or nAg ($p > 0.05$). However, the flexural modulus of the PMMA cements decreased with increasing GS addition compared to that with increasing nAg loading. Most likely because of the lack of agglomeration and uniform distribution of nAg, the mechanical properties of the related subsample were not negatively impacted [48]. Returning to GS, the –NH groups within its structure could hinder intermolecular interactions by increasing the spacing between polymer chains and decreasing chain entanglement. Gentamicin appears to decrease mechanical properties, likely due to the presence of gentamicin domains that could act as flaws, potentially serving as points from which ruptures are initiated [49]. Additionally, gentamicin may form aggregates that can act as stress concentration points within bone cement, reducing compressive and flexural strength [50]. Despite their antibacterial properties, antibiotics such as GS are not favored in clinical practice because of their adverse effects on the mechanical properties of bone cement [51,52].

In this study, on average, the nAg-loaded cement reached the dough state more quickly than the GS-loaded or PMMA BC. Adding nAg to the bone cement apparently accelerated the initiation of polymerization. Furthermore, GS-loaded BC reached dough consistency earlier than nAg-loaded BC did ($p < 0.01$).

In clinical practice, cement is placed at an operation site after doughing, and an implant is inserted before the cement sets. In this situation, a short working time limits the elution of nAg-loaded cement compared with that of GS-loaded cement. Nonetheless, many studies have reported that the antibacterial effect of nAgs is quite strong relative to that of GSs. Moreover, although the setting time might be short, it is still long enough to give the surgeon sufficient working time. Overall, according to the results of this study, the addition of nAg seems to better meet the ISO standard requirements for doughing and setting time. For this reason, the use of nAgs

would still be advantageous considering the potential for antibiotic resistance.

The maximum temperature attained during the hardening of BC should not exceed 90 ± 5 °C. Silver-based antimicrobial agents have also garnered much attention in this regard. In addition to being heat stable, active Ag^+ nanoparticles are nontoxic to human cells and constitute durable biocides owing to their low volatility. In this context, although there are many studies on the antibacterial effect of adding silver to BC [13,19,20,22,37,46,48,53,54], no study has evaluated its exothermic performance. This was confirmed in the present study (Table 2 and Fig. 4), where PMMA cement specimens containing nAg exhibited, on average, lower maximum temperatures during polymerization than did those loaded with GS or $BaSO_4$ (nonloaded) *($p < 0.05$)*. Notably, the temperature difference is greater when nanoparticles are present instead of when conventional (or micron-sized) particles are present. The specimens loaded with nAg had the lowest mean exothermic temperature, 61.37 °C. This was probably due to a weakening of inter- and intramolecular forces within the polymer matrix upon the incorporation of nanoparticles therein [55]. On the other hand, the average maximum curing temperature of the GS-loaded cement was 80.8 °C, which was significantly greater than those of the two other subsamples *($p < 0.05$)*. Polymerization exotherms are inevitable in the polymerization of methacrylate monomers because the bond energy of the –NH group of gentamicin sulfate is greater than that of the C=C groups in MMA. The finding that both nonloaded and nAg-loaded BC had lower exothermic temperatures than GS-loaded BC could be due to the presence of –NH groups in GS as opposed to MMA, which could reduce the concentration of double bonds in the liquid component [56]. Moreover, the hydrophilic nature of GS prevents MMA from dissolving and dispersing homogeneously; GS tends to agglomerate within the structure [57]. Taken together, these findings suggest that adding nAgs can positively and significantly affect the thermal properties of bone cement. Moreover, because high polymerization could also cause necrosis in the application area, the addition of nAg could be a better alternative for preventing such complications than the addition of antibiotics.

Several limitations inherent to the current study should be acknowledged. First, cement from only one brand (BetaCem) was used. Other commercially available products with different viscosities or formulations could yield different results. Second, only hand-mixing was conducted in this study. However, as stated in the literature, different mixing techniques can affect the mechanical properties and porosity of acrylic bone cement [58,59]. Third, antibacterial properties were not evaluated as part of this research since there is already ample related literature. Due to the scope of the present project, antibacterial efficiency testing was not conducted. Despite these limitations, this study marks an inaugural attempt at furnishing an intricate delineation of the mechanical and physical attributes of acrylic cement enhanced with nAg compared to those of gentamicin sulfate.

5. Conclusions

The aim of this study was to compare the effects of nanosilver and gentamicin sulfate on the mechanical and physical properties of acrylic bone cement. Research has demonstrated that acrylic bone cement can be loaded with silver nanoparticles without decreasing its mechanical and handling properties. The resulting bone cement exhibited sound mechanical and physical properties that were better than or not essentially different from those of standard cement, GS-loaded cement or minimum ISO requirements.

Within the limitations of the current study, it can be concluded that when nAg is added to polymethyl methacrylate bone cement, (1) the exothermic temperature is significantly lower, and (2) the compressive and flexural strengths are not adversely affected. These results imply that, considering its mechanical and physical properties, nAg-loaded cement has high potential for use in primary arthroplasty, where antibiotic resistance is a concern. Bone cement containing nanosilver could be a better option than that loaded with conventional antibiotics.

Ethics approval and consent to participate

Not applicable.

Consenpt for publication

Not applicable.

Data availability statement

The datasets generated and/or analyzed during the current study are provided in the Results section of this study.

Funding

This research received no external funding.

CRediT authorship contribution statement

Aysu Aydınoğlu: Writing – review & editing, Writing – original draft, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The author(s) have no conflicts of interest relevant to this article.

Acknowledgements

I would like to thank Betatech Medical Co., Ltd., for donating the bone cement kits used in this study.

References

[1] K.A. Pacheco, Allergy to surgical implants, J. Allergy Clin. Immunol. Pract. 3 (2015) 683–695, https://doi.org/10.1016/j.jaip.2015.07.011.
[2] M. Haque, M. Sartelli, J. McKimm, M.A. Bakar, Health care-associated infections–an overview, Infect. Drug Resist. (2018) 2321–2333.
[3] A. Robu, R. Ciocoiu, A. Antoniac, I. Antoniac, A.D. Raiciu, H. Dura, N. Forna, M.B. Cristea, I.D. Carstoc, Bone cements used for hip prosthesis fixation: the influence of the handling procedures on functional properties observed during in vitro study, Materials 15 (2022) 2967.
[4] M. Wekwejt, A. Michno, K. Truchan, A. Pałubicka, B. Świeczko-Żurek, A.M. Osyczka, A. Zieliński, Antibacterial activity and cytocompatibility of bone cement enriched with antibiotic, nanosilver, and nanocopper for bone regeneration, Nanomaterials 9 (2019), https://doi.org/10.3390/nano9081114.
[5] J.A. Inzana, E.M. Schwarz, S.L. Kates, H.A. Awad, Biomaterials approaches to treating implant-associated osteomyelitis, Biomaterials 81 (2016) 58–71.
[6] V. Alt, T. Bechert, P. Steinrücke, M. Wagener, P. Seidel, E. Dingeldein, E. Domann, R. Schnettler, An in vitro assessment of the antibacterial properties and cytotoxicity of nanoparticulate silver bone cement, Biomaterials 25 (2004) 4383–4391, https://doi.org/10.1016/j.biomaterials.2003.10.078.
[7] M. Miola, A. Bistolfi, M.C. Valsania, C. Bianco, G. Fucale, E. Verné, Antibiotic-loaded acrylic bone cements: an in vitro study on the release mechanism and its efficacy, Mater. Sci. Eng. C 33 (2013) 3025–3032, https://doi.org/10.1016/j.msec.2013.03.032.
[8] M. Ferreira, O. Rzhepishevska, L. Grenho, D. Malheiros, L. Gonçalves, A.J. Almeida, L. Jordão, I.A. Ribeiro, M. Ramstedt, P. Gomes, A. Bettencourt, Levofloxacin-loaded bone cement delivery system: highly effective against intracellular bacteria and Staphylococcus aureus biofilms, Int J Pharm 532 (2017) 241–248, https://doi.org/10.1016/j.ijpharm.2017.08.089.
[9] D. Neut, E.P. de Groot, R.S.Z. Kowalski, J.R. van Horn, H.C. van der Mei, H.J. Busscher, Gentamicin-loaded bone cement with clindamycin or fusidic acid added: biofilm formation and antibiotic release, J. Biomed. Mater. Res. Part A: An Official Journal of The Society for Biomaterials, The Japanese Society for Biomaterials, and The Australian Society for Biomaterials and the Korean Society for Biomaterials 73 (2005) 165–170.
[10] J. Slane, B. Gietman, M. Squire, Antibiotic elution from acrylic bone cement loaded with high doses of tobramycin and vancomycin, Journal of Orthopaedic Research® 36 (2018) 1078–1085.
[11] Y. Chang, C.L. Tai, P.H. Hsieh, S.W.N. Ueng, Gentamicin in bone cement: a potentially more effective prophylactic measure of infection in joint arthroplasty, Bone Joint Res 2 (2013) 220–226.
[12] L. Paiva, T.K.S. Fidalgo, L.P. Da Costa, L.C. Maia, L. Balan, K. Anselme, L. Ploux, R. Thiré, Antibacterial properties and compressive strength of new one-step preparation silver nanoparticles in glass ionomer cements (NanoAg-GIC), J. Dent. 69 (2018) 102–109.
[13] L. Muñoz, L. Tamayo, M. Gulppi, F. Rabagliati, M. Flores, M. Urzúa, M. Azócar, J.H. Zagal, M. V Encinas, X. Zhou, Surface functionalization of an aluminum alloy to generate an antibiofilm coating based on poly (methyl methacrylate) and silver nanoparticles, Molecules 23 (2018) 2747.
[14] K. Zheng, M.I. Setyawati, D.T. Leong, J. Xie, Antimicrobial silver nanomaterials, Coord. Chem. Rev. 357 (2018) 1–17.
[15] S.-C. Shen, K. Letchmanan, P.S. Chow, R.B.H. Tan, Antibiotic elution and mechanical property of TiO2 nanotubes functionalized PMMA-based bone cements, J. Mech. Behav. Biomed. Mater. 91 (2019) 91–98.
[16] B. Świeczko-Żurek, A. Zieliński, D. Bociąga, K. Rosińska, G. Gajowiec, Influence of different nanometals implemented in PMMA bone cement on biological and mechanical properties, Nanomaterials 12 (2022), https://doi.org/10.3390/nano12050732.
[17] A. Zaharia, V. Muşat, V.P. Ghisman, N. Baroiu, Antimicrobial hybrid biocompatible materials based on acrylic copolymers modified with (Ag) ZnO/chitosan composite nanoparticles, Eur. Polym. J. 84 (2016) 550–564.
[18] Q.H. Tran, A.-T. Le, Silver nanoparticles: synthesis, properties, toxicology, applications and perspectives, Adv. Nat. Sci. Nanosci. Nanotechnol. 4 (2013) 033001.
[19] H.F. Elsherif, S.H. Saniour, I.T. Motawea, H.A. Essawy, M.M. Abd El-Gany, D.Y. Zaki, Preparation, characterization and evaluation of a poly methyl methacrylate bone cement modified by montmorillonite loaded with silver nano particles, Al-Azhar Dental Journal for Girls 9 (2022) 441–450, https://doi.org/10.21608/adjg.2022.76299.1391.
[20] P. Prokopovich, M. Köbrick, E. Brousseau, S. Perni, Potent antimicrobial activity of bone cement encapsulating silver nanoparticles capped with oleic acid, J. Biomed. Mater. Res. B Appl. Biomater. 103 (2015) 273–281.
[21] F. Okafor, A. Janen, T. Kukhtareva, V. Edwards, M. Curley, Green synthesis of silver nanoparticles, their characterization, application and antibacterial activity, Int J Environ Res Public Health 10 (2013) 5221–5238.
[22] J.S. Kim, E. Kuk, K.N. Yu, J.-H. Kim, S.J. Park, H.J. Lee, S.H. Kim, Y.K. Park, Y.H. Park, C.-Y. Hwang, Antimicrobial effects of silver nanoparticles, Nanomedicine 3 (2007) 95–101.
[23] F. Martinez-Gutierrez, P.L. Olive, A. Banuelos, E. Orrantia, N. Nino, E.M. Sanchez, F. Ruiz, H. Bach, Y. Av-Gay, Synthesis, characterization, and evaluation of antimicrobial and cytotoxic effect of silver and titanium nanoparticles, Nanomedicine 6 (2010) 681–688.
[24] O. Choi, K.K. Deng, N.-J. Kim, L. Ross Jr., R.Y. Surampalli, Z. Hu, The inhibitory effects of silver nanoparticles, silver ions, and silver chloride colloids on microbial growth, Water Res. 42 (2008) 3066–3074.
[25] K. Kalishwaralal, S. BarathManiKanth, S.R.K. Pandian, V. Deepak, S. Gurunathan, Silver nanoparticles impede the biofilm formation by Pseudomonas aeruginosa and Staphylococcus epidermidis, Colloids Surf. B Biointerfaces 79 (2010) 340–344.
[26] S. Mohanty, S. Mishra, P. Jena, B. Jacob, B. Sarkar, A. Sonawane, An investigation on the antibacterial, cytotoxic, and antibiofilm efficacy of starch-stabilized silver nanoparticles, Nanomedicine 8 (2012) 916–924.
[27] I.S.O. Standard, 5833: 2002; Implants for Surgery—Acrylic Resin Cements, International Standards Organization, Geneva, Switzerland, 2002.
[28] A. Standard, ASTM F451: standard specification for acrylic bone cement, Annu. Book ASTM (Am. Soc. Test. Mater.) Stand. 13 (1) (2000) 55–61. West Conshohocken, PA: ASTM.
[29] R. Karpiński, J. Szabelski, J. Maksymiuk, Seasoning polymethyl methacrylate (PMMA) bone cements with incorrect mix ratio, Materials 12 (2019) 3073.
[30] J.H. Tan, B.T.H. Koh, A.K. Ramruttun, W. Wang, Compression and flexural strength of bone cement mixed with blood, J. Orthop. Surg. 24 (2016) 240–244.
[31] J. Szabelski, R. Karpiński, P. Krakowski, M. Jojczuk, J. Jonak, A. Nogalski, Analysis of the effect of component ratio imbalances on selected mechanical properties of seasoned, medium viscosity bone cements, Materials 15 (2022) 5577.
[32] S. Gamal, M. Mikhail, N. Salem, M.T. EL-Wakaad, R. Abdelbaset, Effect of Using Nano-Particles of Magnesium Oxide and Titanium Dioxide to Enhance Properties of Hip Joint Bone Cement, 2023.
[33] A.-M. Yousefi, A review of calcium phosphate cements and acrylic bone cements as injectable materials for bone repair and implant fixation, J. Appl. Biomater. Funct. Mater. 17 (2019) 2280800019872594, https://doi.org/10.1177/2280800019872594.
[34] H.A. Samad, M. Jaafar, R. Othman, M. Kawashita, N.H.A. Razak, New bioactive glass-ceramic: synthesis and application in PMMA bone cement composites, Bio Med. Mater. Eng. 21 (2011) 247–258.
[35] S. He, C. Scott, M. De Luise, B. Edwards, P. Higham, Effect of choice of surgical gloves on dough time measurements of acrylic bone cement, Biomaterials 24 (2003) 235–237.

[36] M. Wekwejt, N. Moritz, B. Świeczko-Żurek, A. Pałubicka, Biomechanical testing of bioactive bone cements – a comparison of the impact of modifiers: antibiotics and nanometals, Polym. Test. 70 (2018) 234–243, https://doi.org/10.1016/j.polymertesting.2018.07.014.
[37] A. Robu, A. Antoniac, R. Ciocoiu, E. Grosu, J. V Rau, M. Fosca, I.I. Krasnyuk, G.G. Pircalabioru, V. Manescu Paltanea, I. Antoniac, S. Gradinaru, Effect of the antimicrobial agents peppermint essential oil and silver nanoparticles on bone cement properties, Biomimetics 7 (2022), https://doi.org/10.3390/biomimetics7030137.
[38] G. Frutos, J.Y. Pastor, N. Martínez, M.R. Virto, S. Torrado, Influence of lactose addition to gentamicin-loaded acrylic bone cement on the kinetics of release of the antibiotic and the cement properties, Acta Biomater. 6 (2010) 804–811.
[39] A.B. Welch, Antibiotics in acrylic bone cement. In vitro studies, J. Biomed. Mater. Res. 12 (1978) 679–700.
[40] S. Cavalu, Acrylic bone cements: new insight and future perspective, Key Eng. Mater. 745 (2017) 39–49.
[41] K.-D. Kühn, Bone Cements: Up-To-Date Comparison of Physical and Chemical Properties of Commercial Materials, Springer Science & Business Media, 2012.
[42] V.A. Williams, T.G. Ribelli, P. Chmielarz, S. Park, K. Matyjaszewski, A silver bullet: elemental silver as an efficient reducing agent for atom transfer radical polymerization of acrylates, J. Am. Chem. Soc. 137 (2015) 1428–1431.
[43] K.-D. Kühn, N. Renz, A. Trampuz, Local antibiotic therapy, Unfallchirurg 120 (2017) 561–572.
[44] I.S.O. Standard, 5833: 2002; Implants for Surgery—Acrylic Resin Cements, International Standards Organization, Geneva, Switzerland, 2002.
[45] Z. Shi, K.G. Neoh, E.T. Kang, W. Wang, Antibacterial and mechanical properties of bone cement impregnated with chitosan nanoparticles, Biomaterials 27 (2006) 2440–2449, https://doi.org/10.1016/j.biomaterials.2005.11.036.
[46] A. Sodagar, M.Z. Kassaee, A. Akhavan, N. Javadi, S. Arab, M.J. Kharazifard, Effect of silver nano particles on flexural strength of acrylic resins, J Prosthodont Res 56 (2012) 120–124.
[47] E.P. Lautenschlager, J.J. Jacobs, G.W. Marshall, P.R. Meyer Jr., Mechanical properties of bone cements containing large doses of antibiotic powders, J. Biomed. Mater. Res. 10 (1976) 929–938.
[48] P. Prokopovich, R. Leech, C.J. Carmalt, I.P. Parkin, S. Perni, A novel bone cement impregnated with silver–tiopronin nanoparticles: its antimicrobial, cytotoxic, and mechanical properties, Int J Nanomedicine 8 (2013) 2227.
[49] Y. He, J.P. Trotignon, B. Loty, A. Tcharkhtchi, J. Verdu, Effect of antibiotics on the properties of poly(methylmethacrylate)-based bone cement, J. Biomed. Mater. Res. 63 (2002) 800–806, https://doi.org/10.1002/jbm.10405.
[50] I.-C. Chen, C.-Y. Su, W.-H. Nien, T.-T. Huang, C.-H. Huang, Y.-C. Lu, Y.-J. Chen, G.-C. Huang, H.-W. Fang, Influence of antibiotic-loaded acrylic bone cement composition on drug release behavior and mechanism, Polymers 13 (2021) 2240.
[51] S.-C. Shen, W.K. Ng, Y.-C. Dong, J. Ng, R.B.H. Tan, Nanostructured material formulated acrylic bone cements with enhanced drug release, Mater. Sci. Eng. C 58 (2016) 233–241, https://doi.org/10.1016/j.msec.2015.08.011.
[52] T. Thielen, S. Maas, A. Zuerbes, D. Waldmann, J. Kelm, Mechanical material properties of polymethylmethacrylate (PMMA) for medical applications, Mater. Test. 51 (2009) 203–209.
[53] A. Robu, A. Antoniac, E. Grosu, E. Vasile, A.D. Raiciu, F. Iordache, V.I. Antoniac, J. V Rau, V.G. Yankova, L.M. Ditu, Additives imparting antimicrobial properties to acrylic bone cements, Materials 14 (2021) 7031.
[54] J. Slane, J. Vivanco, W. Rose, H.-L. Ploeg, M. Squire, Mechanical, material, and antimicrobial properties of acrylic bone cement impregnated with silver nanoparticles, Mater. Sci. Eng. C 48 (2015) 188–196, https://doi.org/10.1016/j.msec.2014.11.068.
[55] A. Köroğlu, O. Şahin, I. Kürkçüoğlu, D.Ö. Dede, T. Özdemir, B. Hazer, Silver nanoparticle incorporation effect on mechanical and thermal properties of denture base acrylic resins, J. Appl. Oral Sci. 24 (2016) 590–596.
[56] W. Zhu, F. Liu, B. Yu, J. He, Preparation of antibacterial acrylic bone cement with methacrylate derived from benzothiazole, J. Mech. Behav. Biomed. Mater. 117 (2021) 104403, https://doi.org/10.1016/j.jmbbm.2021.104403.
[57] E. Scholar, Gentamicin, in: S.J. Enna, D.B. Bylund (Eds.), XPharm: the Comprehensive Pharmacology Reference, Elsevier, New York, 2007, pp. 1–6, https://doi.org/10.1016/B978-008055232-3.61821-5.
[58] N.J. Dunne, J.F. Orr, Influence of mixing techniques on the physical properties of acrylic bone cement, Biomaterials 22 (2001) 1819–1826, https://doi.org/10.1016/S0142-9612(00)00363-X.
[59] S. Ferraris, M. Miola, A. Bistolfi, G. Fucale, M. Crova, A. Massé, E. Verné, In vitro comparison between commercially and manually mixed antibiotic-loaded bone cements, J. Appl. Biomater. Biomech. 8 (2010) 166–174.