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Research Article

Preparation and Assessment of Physicochemical Possessions, Solubility, and Antimicrobial Properties of Dental Prosthesis Glass Ionomer Cement Containing Curcumin Nanocrystals

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The physicochemical, antibacterial, and mechanical properties of the cement used in fixed dental prostheses show particular importance in the successful treatment. The objective of this in vitro study was to prepare glass ionomer cements (GIC) containing curcumin nanocrystals, as a sealant between the prepared tooth and crown. The prepared cements containing curcumin nanocrystals with concentration of 20% and 30% were evaluated by conventional physicochemical methods, and then, the effects of adding nanocrystals on the cement water solubility and sorption were measured. Finally, the antibacterial effects of the prepared cement were evaluated against three bacterial strains of *Streptococcus mutans*, *Staphylococcus aureus*, and *Escherichia coli*. The results showed that the solubility and sorption of both GIC containing curcumin nanocrystals did not change significantly compared with the control ($p > 0.05$). The cement containing 20% and 30% curcumin nanocrystals showed significant increase in antibacterial effect ($p < 0.05$). Considering the suitable physicochemical properties and worthy antibacterial result GIC containing curcumin nanocrystals, it seems that it can be a suitable restorative material.

1. Introduction

Loss of the attachment between the restoration and the tooth causes microleakage which eventually leads to secondary caries and inflammatory irritation of pulp [1]. Traditionally, cements, such as glass ionomer cements (GIC), are utilized to fill gaps and have been used as sealing agents between the tooth preparation and crown. Unfortunately, although cements are considered to seal the margins of the crown, microleakage of bacteria may occur, leading to secondary decay and thus the durability of the restoration. However, several laboratory studies have confirmed that GICs have an antibacterial effect. These antibacterial properties are related to the release of fluoride that is believed to prevent bacterial growth. However, fluoride is released over a short period of time and the antibacterial activity wears off over time [2]. Microleakage is a prevalent clinical phenomenon through which oral fluids, molecules, ions, and bacteria penetrate the interface of tooth restoration and access the dentinal tubules and pulp [3]. Restoration margins are a potential route for leakage of cariogenic microorganisms that exist in normal human flora [4].

Two groups of bacteria are responsible for caries: *Streptococcus mutans* and *Lactobacillus casei*. Increased levels of

these bacteria have been described in caries plaques [5]. Caries-causing bacteria, such as *Streptococcus mutans*, efficiently break down fermentable carbohydrates to acids, which can destroy the tooth tissue [3].

There are no definite criteria for judging the complete removal of caries during preparation. Residual bacteria of caries lesions have also been shown to increase pulp susceptibility, inflammation, and secondary caries. Antibacterial effect of dental cements, during and after the setting, assumes clinical relevance, because this effect may help in the eradication or decrease of bacteria that have persisted viable on preparation walls or bacteria that may gain access to the cavity via microleakage fissures [3]. A perfect luting material should have basic biological, mechanical, and handling prerequisites including adequate working time, biocompatibility, compressive strength, low solubility in oral fluids, flowability, adhesiveness, minimum microleakage, low cost, esthetics, and ease of removal in case of excess material. No single luting agent is able of meeting all the stringent requirements [6].

The GIC was designed in the late 1960s [7]. GIC binds well to the tooth enamel and to some extent to the dentin, releasing fluoride at the same time. Originally used as a restorative material, GICs are increasingly used as luting agents, liners, bases, gap sealants, and fillers in the atraumatic restorative treatment (ART) method [6]. Drying of moisture and sensitivity to early contamination, which causes the integrity of the material, is the main concern of this cement [6].

Recently, nanotechnology has found many applications in the various sciences [8–12]. The discipline of nanotechnology comprises the study of nanoparticles that can be classified as particles with a size no greater than 100 nm. These particles with an antimicrobial effect have received extensive attention within a range of different fields such as medicine and dentistry [13]. Properties of nanoparticles, their active surface area, the biological action, and the chemical reactivity are often completely different from particles of a greater size [14]. Various nanoparticles have become popular in dentistry and medicine as antimicrobial agents [15]. The higher surface-to-volume ratio and charge density result in their greater interaction with the environment, which leads to their higher antibacterial activity [15]. To improve effective antimicrobial and antioxidant therapies, the greatest plan may be to create novel nanoscale drug delivery systems [16].

GICs containing nanopaticulated antimicrobial agents have been investigated for improving the antimicrobial properties of GICs [17–19].

Curcumin, a polyphenolic agent and important component of *Curcuma longa* L., is well known for its numerous biological effects such as anti-inflammatory, antioxidant, and antibacterial activities [20–26]. In addition to strong biological activity, curcumin suffers from pharmacokinetic problems such as low solubility, low bioavailability, poor absorption, and immediate metabolism in the human body, which limits its clinical application. To solve these problems, investigators utilized the wet-milling method to prepare nanosized curcumin particles that increased their surface area, which increased the dissolution rate in water and increased its physical and chemical stability [27, 28].

As mentioned, the antibacterial properties of cements used in fixed prostheses are of particular importance in the success of treatment; however, studies have shown that cements on the market do not have such properties. The aim of this in vitro study was to prepare a cement containing curcumin nanocrystals, which is used as a sealant between the prepared tooth and the crown, and examine the effect of this cement against three bacterial species *E. coli*, *S. aureus*, and *S. mutans*.

2. Materials and Methods

2.1. Synthesis of Nanosized Curcumin. The curcumin nanocrystals were prepared according to our previous study [29]. To prepare nanocurcumin, curcumin powder was dissolved in 100 ml of dichloromethane to make a 50 mg/ml concentration solution. Then, distilled water (5 ml) was drop wised to the solution under ultrasonic conditions with an ultrasonic source at a frequency of 50 kHz for 30 minutes. The resulting solution was then mixed at 800 rpm for 20 minutes on a magnetic stirrer to obtain an orange precipitate. Twin 80 (1%) was used as a surfactant. After evaporation of organic solvent in the operator, the precipitate was separated from the supernatant by centrifugation at high speed (20000 rpm) and dried by an oven.

2.2. Preparation of Cement Powder Containing Nanocurcumin. GC Fuji I (GC Corporation/Itabashi-CHO, Tokyo, Japan) was physically mixed with curcumin nanocrystals powder with weight percentages of 80 to 20 and 70 to 30. For standard mixing of cement powder and nanoparticle powder, each of them was weighed accurately with a digital balance (AND, HR20, UK) with an accuracy of 0.0001 and then the specified weight percentages of them were mixed in a minimixer. Mixing was continued to ensure complete mixing of the ingredients.

2.3. Characterization of Nanoparticles and Physicochemical Studies. The prepared powders were subjected to the physicochemical studies. Fourier transmission infrared spectroscopy (FTIR) was used to investigate possible connections and identification of functional groups, X-ray diffraction (XRD) (Siemens, Model D5000, Germany) was used to evaluate characteristics of crystallinity and scanning electron microscopy (SEM, TESCAN, Warrendale, PA) together the energy dispersive X-ray (EDAX) was used to examine the morphology and the percentage of nanocurcumin in the prepared nanomaterial. The standard concentration curcumin concentration inside the cement was prepared by UV spectrophotometer (Shimadzo, Japan) and the release pattern of curcumin from the cement matrix structure was evaluated by drug dissolution devices (USP apparatus II, paddle stirrer) and UV spectrophotometer.

To measure the release outline of curcumin from the prepared material, it was put under magnetic streaming in 100 ml of phosphate buffer medium (100 rpm, temperature of 37°C, and pH of 7.4). At different time points (2, 4, 6, 8,

10, and 12 days), 1 ml of the medium was collected and then replaced with the same volume of primary buffer medium without curcumin. The amount of curcumin was then measured by ultraviolet spectrophotometry at 350 nm for each point. Curcumin concentration was calculated using a standard curve and the release pattern was explained.

2.4. Solubility (Wsl) and Water Sorption (Wsp). For solubility and water sorption test, materials were prepared according to the International Organization for Standards (ISO) specification 4049: 2009 [30]. First, a thin and transparent layer of glass was placed on the metal molds (15 mm in diameter and 1 mm in height). The curcumin cement powder was prepared in the previous step (with weight percentages of 80 to 20 and 70 to 30) mixed with cement liquid based on the manufactory direction (15 g powder with 8 ml liquid). Prepared cements were put into metal molds and covered with a second transparent layer on the samples. The samples were incubated at 37°C for 15 minutes. They were then placed in light-proof boxes for one hour. Samples were taken out and carefully removed from molds. Cement excesses were removed from the margins of the samples and the samples were polished to remove irregularities and additions of cement. For this purpose, the samples were drawn on sandpaper no. 1 by rotating motion. Debris from wear of the samples was cleaned using compressed air powder. Finally, the diameter of the samples after polishing should not be less than 14.8 mm. Three samples were prepared from each cement in this way. Samples were placed at least 3 mm apart in the first desiccator containing silica gel and kept at 37°C for 22 hours. After 22 hours, the samples entered the second desiccator at a temperature of 23°C for 2 hours.

Samples were weighed and the drying process was continued until the weight of the samples was fixed at weight M1 (until the weight change of the samples during the 24-hour cycle was less than 0.1 mg). The weight of the samples reached a constant weight of M1. The final sample size was also measured after the samples reached M1. The volume of the samples was measured with a specified height (h) and a known diameter (D) (with a measurement accuracy of 0.01 mm). The mean diameter is the average size of two diameters perpendicular to each other, and the mean height of each sample is the average height at 5 points (one in the center and four points apart in the sample environment). The volume of each sample was obtained using the mean values of diameter and height.

Samples were placed in distilled water in a volume of at least 10 ml and placed in an incubator at 37° C for 7 days. After 7 days, the samples were removed and washed with fresh distilled water and dried with paper until the water was not visible on the surface of the samples and was shaken in the air for 15 seconds before being removed for one minute. Samples were passed through the incubator; their weight was measured (M2). The drying cycle process was repeated on the samples in desiccator containing silica gel for 5 weeks, as described for the weight of the samples to reach M1. The final and proven weights of the samples were finally measured (M3).

The degree of solubility and water absorption was obtained according to the formulas described in the ISO4049 standard [30].

$$\mathrm{Wsp} = \frac{(\mathrm{M2} - \mathrm{M3})}{\mathrm{V2}}, \quad (1)$$

$$\mathrm{Wsl} = \frac{(\mathrm{M1} - \mathrm{M3})}{\mathrm{V2}}. \quad (2)$$

2.5. Antimicrobial Test. Bacterial strains, *S. aureus* (ATCC: 6538), *E. coli* (ATCC: 25922) and *S. mutans* (ATCC 25175), were prepared as reference strains from the Pasteur Institute of Iran. To investigate the antibacterial effect of curcumin nanoparticles, the disk diffusion test was used. For this purpose, a suspension of curcumin nanoparticles in water was prepared. Different dilutions were prepared and then mixed with the Mueller-Hinton Broth medium in microplate wells. The vancomycin (30 mg per disk) and tetracycline (30 mg per disk) were used as the positive control to compare growth inhibition zones. Cement containing curcumin nanocrystals and cement without curcumin (negative control) were prepared as disks with a diameter of 6 mm. Then, the Mueller-Hinton agar culture medium was prepared in microbiological plates. The sterile swab was immersed in a microbial suspension with a concentration of half McFarland (1.5×10^8 cfu) and then grassed three times at the plate surface at a 60 degree angle; then, the swab was rotated around the inner part of the plate. Then, the disks were placed separately on the culture medium and after 24 hours of incubation at 35°C, finally, the diameter of the growth inhibition zone around the disks was measured.

2.6. Statistical Analysis. To compare the findings among the investigated groups, a one-way analysis of variance was employed (GraphPad Prism software, version 9). Significance level of test was considered 0.05.

3. Results and Discussion

Figure 1 shows the SEM image together with the energy dispersive X-ray (EDAX) for the prepared materials.

Figure 2 shows the results for XRD test for the prepared materials. No apparent peak was observed in the pattern of X-ray diffraction. This is due to the amorphous nature of glass ionomer powder [31]. The lower XRD peak intensities in Glass Ionomer cement containing 20% nanocurcumin and Glass Ionomer cement containing 30% nanocurcumin is related to the presence of curcumin nanocrystals in the cement matrix. The lower intensity of the curcumin nanocrystals compared with the bulk curcumin (JCPDS standard card (9-816)) suggests the lower crystallinity and the smaller sizes [32], which was consistent with our SEM results (Figure 1). Khaghani et al. reported the similar results for strontium-containing glass ionomer cement [31].

The results of FTIR test for the prepared samples are presented in Figure 3. FTIR analysis displayed absorptions at 1,720 cm^{-1} for C=O stretching of the ester group, at 1,650 cm-1 for C=O of the ketone group, and at 1,300 cm^{-1}

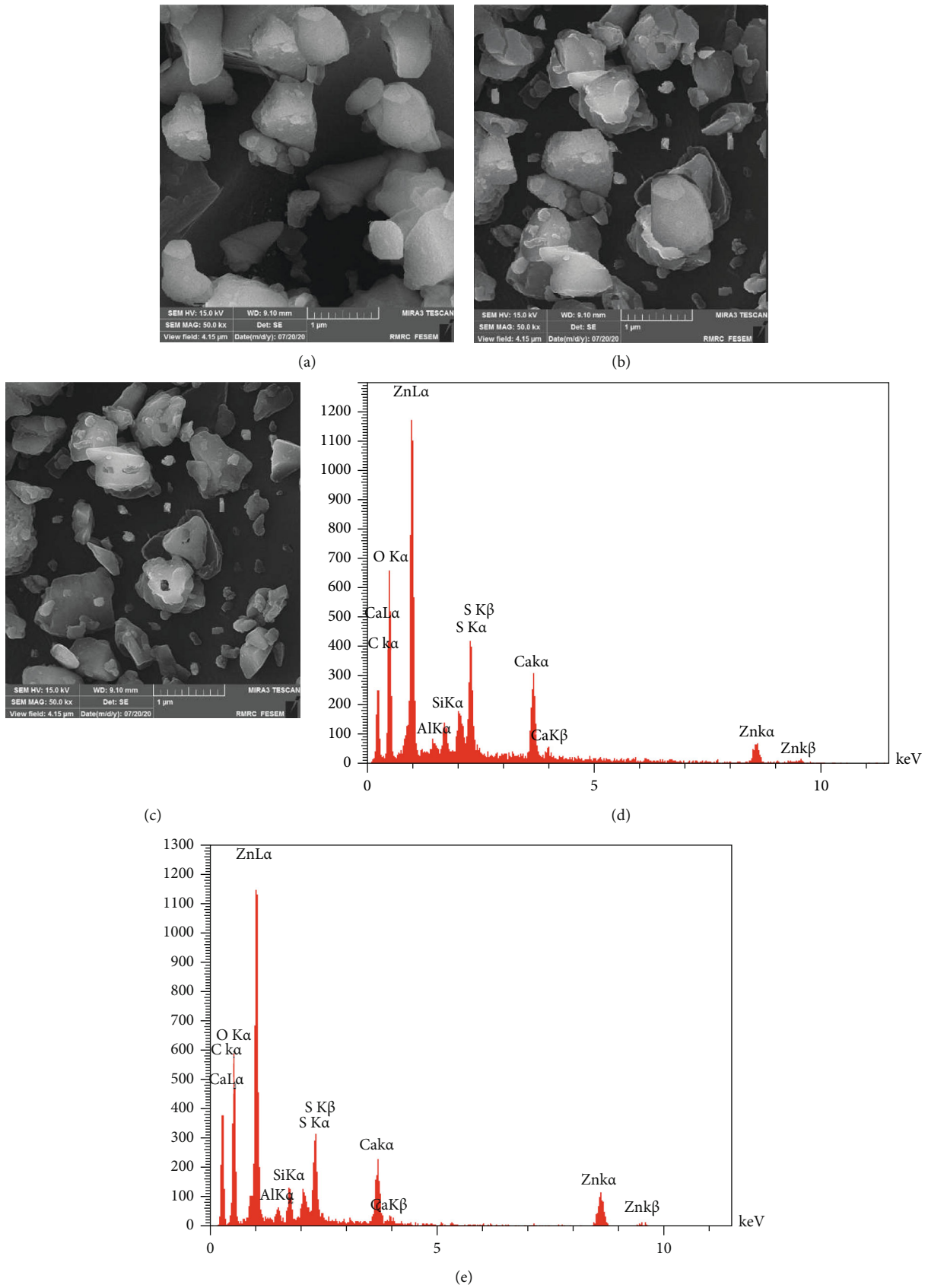

Figure 1: Continued.

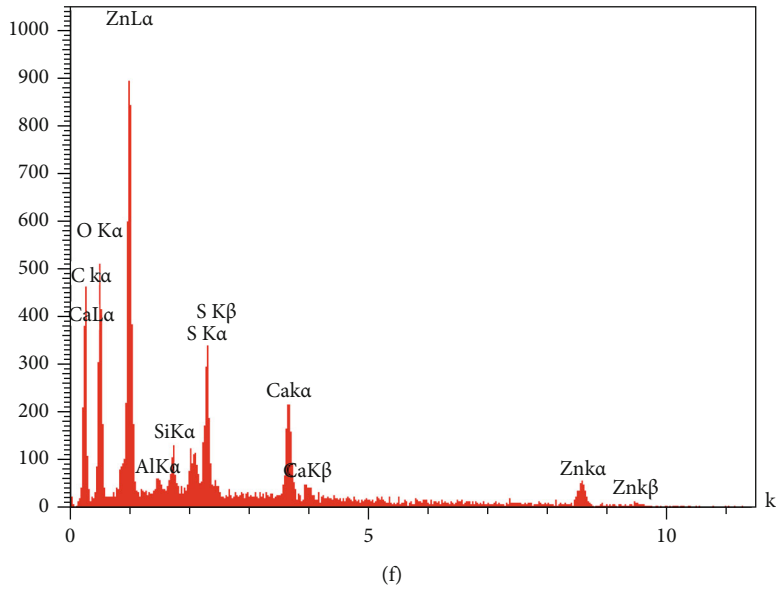

Figure 1: SEM image for Glass Ionomer cement without nanocurcumin (a), Glass Ionomer cement containing 20% nanocurcumin (b) and Glass Ionomer cement containing 30% nanocurcumin (c). SEM magnification is 50.0 kx. The energy dispersive X-ray (EDAX) for Glass Ionomer cement without nanocurcumin (d), Glass Ionomer cement containing 20% nanocurcumin (e), and Glass Ionomer cement containing 30% nano-curcumin (f).

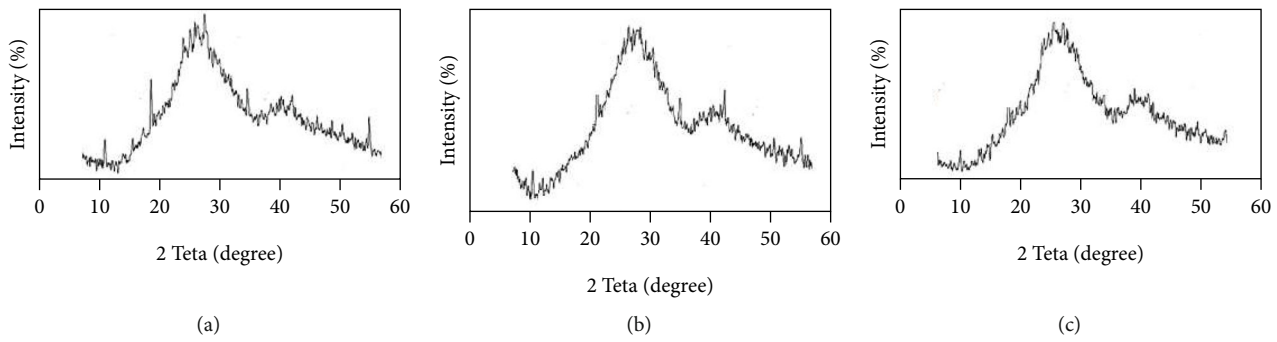

Figure 2: The results for XRD test: Glass Ionomer cement containing 30% nanocurcumin (a), Glass Ionomer cement containing 20% nano-curcumin (b), and Glass Ionomer cement without nanocurcumin (c).

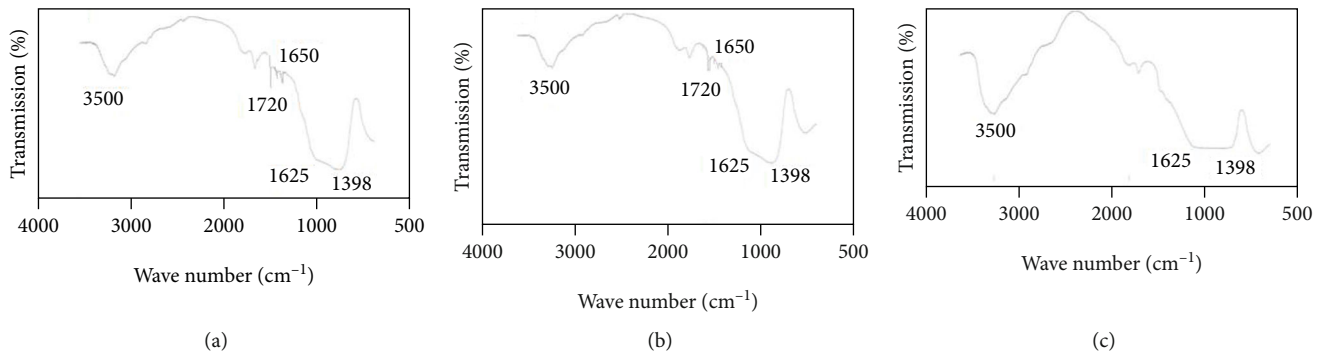

Figure 3: The results for FTIR test: Glass Ionomer cement containing 30% nano-curcumin (a), Glass Ionomer cement containing 20% nanocurcumin (b), and Glass Ionomer cement without nanocurcumin (c).

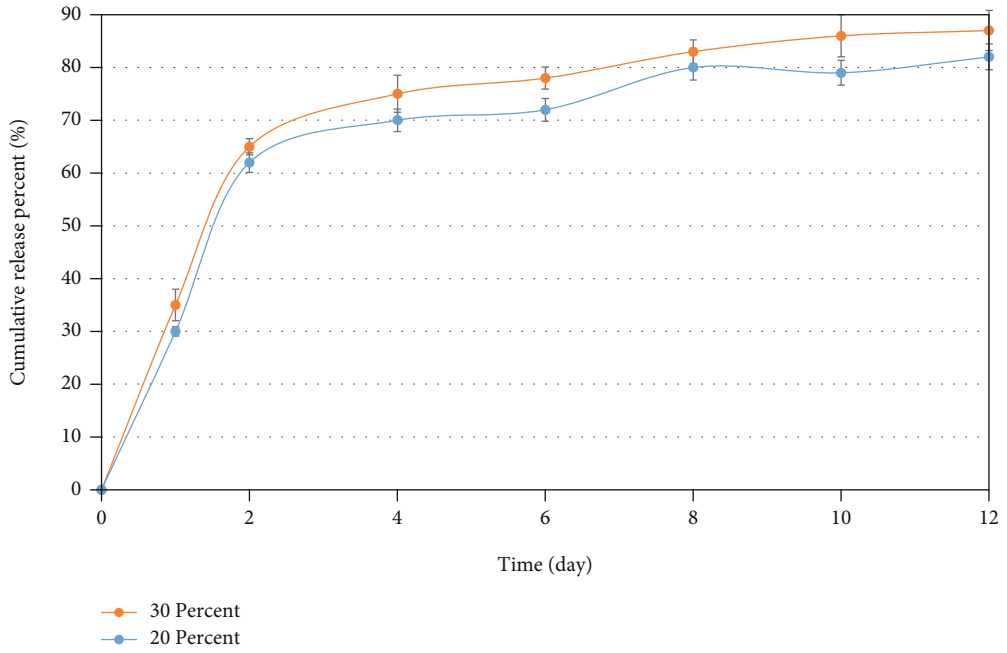

Figure 4: The release profile for the curcumin nanoparticles from Glass Ionomer cement containing 30% nano-curcumin and 20% nano-curcumin.

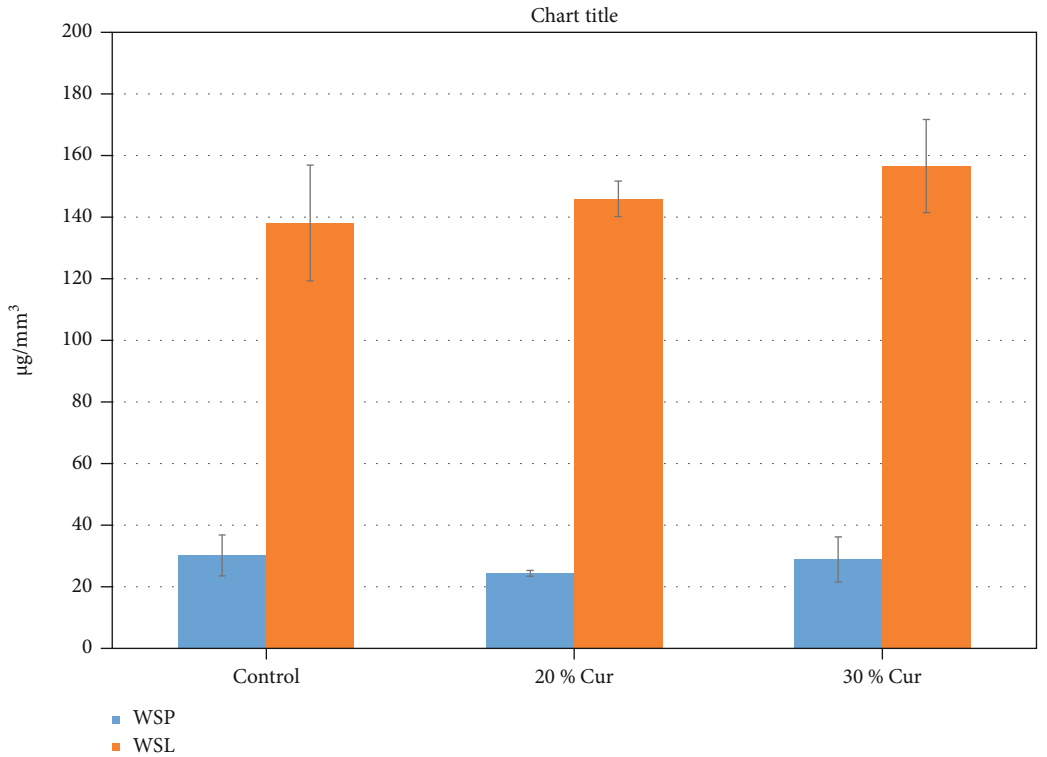

Figure 5: Wsl and Wsp of control (GIC without nanocurcumin), containing 20% and 30% curcumin nanocrystals. The solubility and sorption of both GIC containing curcumin nanocrystals did not change significantly compared with the control ($p > 0.05$).

Table 1: The zone size of control positive, control negative, and cement containing 20% and 30% curcumin nanocrystals against *S. mutans*, *S. aureus*, and *E. coli* (Significant increase in antibacterial effect ($p < 0.05$) compare with the control).

The name of bacteria	Zone size (30%)	Zone size (20%)	Zone size of positive control	Zone size of blank (negative control)
S. mutans	$13.5 \pm 0.5^*$	$12 \pm 0.5^*$	16.5 ± 0.5	0
E. coli	$15.5 \pm 0.5^*$	$14.5 \pm 0.5^*$	11 ± 0	0
S. aureus	$15 \pm 0^*$	$13.5 \pm 0.5^*$	8.5 ± 0.5	0

for the ether group. A sharp band at about 3,500 cm-1 and a broad peak at 3,200-3,500 cm^{-1} in the spectrum have been attributed to the –OH group stretching vibration [33].

The peaks at wavelengths 1398 cm^{-1} and 1625 cm^{-1} are, respectively, related to symmetric and asymmetric tensile vibrations of COO^- (in carboxylic acid salt compounds) in glass ionomer cement powder [31].

The results for the release profile were presented in Figure 4. A burst release of curcumin was observed on the first and second days followed by a gradual release until day 12. A two-stage release kinetics was mainly observed for drug-loaded inorganic materials; a fast-releasing stage and a sustained-release stage. The first stage is a result of the fast transport of initially desorbed molecules, while the second stage is related to the desorption of drug molecules from the inner matrix [34]. In a study by Otsuka, Glass Ionomer cement containing cephalexin showed the similar release profile. According to their results, 30% of the loaded drug was released from the cement at the initial fast stage, and the rest was released more slowly [35]. Kiri et al. also reported two-stage release profile for methotrexate-loaded glass ionomer cements [36].

The data for the degree of solubility and water sorption are shown in Figure 5. Solubility of cement components has a potential impact on both its structural stability and biocompatibility [37]. The solubility of dental restorative materials influences both their biological compatibility and their rate of degradation [38].

In this study, the solubility and sorption of both GIC containing curcumin nanocrystals did not change significantly compared with the control ($p > 0.05$). An increase in solubility of the material may cause cement degradation, leading to debonding of the sealant and a break in the marginal integrity, and cause recurrent decay, which addition of curcumin nanocrystals did not increase the solubility and water sorption of GIC.

In the results of disk diffusion test, cement containing 20% and 30% curcumin nanocrystals showed significant increase in the antibacterial effect ($p < 0.05$) compare with control against *S. mutans*, *S. aureus*, and *E. coli* (Table 1).

The capability to decrease bacterial growing would lower the risk of additional cavitation and demineralization, because caries is an infectious disease and the elimination of cariogenic bacteria is the mainstay of treatment. In the present study, physicochemical properties, solubility, and the antibacterial action of GICs containing nanocurcumin were evaluated.

Our study displayed that the addition of curcumin nanocrystals to GIC enhanced antibacterial properties over the glass ionomer (without curcumin) for *E. coli*, *S. aureus*, and *S. mutans*. This antimicrobial effect of the cements was due to nanocurcumin release. Glass ionomer (without curcumin) showed no bacterial inhibition zone. It was also found that the growth inhibition zone diameter against *S. mutans*, *S. aureus*, and *E. coli* was dependent upon the concentration of incorporated curcumin nanocrystals and GIC containing 30% nanocurcumin had the more antibacterial effect than 20% one. However, this was not significant ($p > 0.05$).

Botelho et al. tested the antimicrobial effect of combining antibacterial agents (chlorhexidine hydrochloride, cetrimide, cetylpyridinium chloride, and benzalkonium chloride) with a glass ionomer cement (GIC) using an agar diffusion test. According to their results, the antibacterial containing GICs presented significant inhibition zone. However, control GIC (without antimicrobial agent) produced no bacterial inhibition zone [39].

Enan et al. tested synergistic effect of GIC containing incorporate silver nanoparticles and amoxicillin on oral microbes. The results showed that GIC had a synergistic effect in combination with amoxicillin and silver nanoparticles against studied microorganisms [40].

In another study, Alrahlah et al. tested the influence of curcumin photosensitizer on caries-affected dentin (CAD) and microleakage to bioactive (BA) and multicore (MC) bulk-fill composite. The results have shown curcumin photosensitizer needs further investigation for clinical use [41].

Al-Hamdan et al. assessed the shear bond strength (SBS) of CAD bonded to a dental glass ionomer cement after being disinfected with curcumin/O_3 and chlorhexidine. Curcumin/O_3 showed improved SBS of cement. Chlorhexidine revealed low microleakage scores with decrease of bond integrity [42].

4. Conclusion and Future Outlooks

Considering the appropriate physicochemical properties, worthy antibacterial effect and no increase of solubility and water sorption in GIC containing curcumin nanocrystals, it seems that it can be as a suitable restorative material. The results showed that the use of new plant antimicrobials could be effective in controlling bacterial infections. There is a need for further laboratory studies on the physicomechanical properties of the new material under study. Extensive cellular, animal, and clinical studies are also needed to demonstrate the function of temporary restorative containing nanocurcumin. The antibacterial properties of restorative dental cements may lead to better prosthesis treatments. Besides, the use of these nanoparticles in optimal formulation and appropriate concentration can replace the use of chemical antimicrobials in the future.

Data Availability

The raw/processed data required to reproduce these findings can be shared after publication by requesting from the corresponding author.

Ethical Approval

This study was approved by the Ethic Committee of the Tabriz University of Medical Sciences (Ethical code: IR.TBZMED.VCR.REC.1399.038).

Conflicts of Interest

The authors state that there are no conflicts of interest.

Authors' Contributions

Sahar Choukhachizadeh Moghaddam and Ramin Negahdari contributed equally to this work.

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