THE STRUCTURE AND SOLUBILITY of SiO_2-Ga_2O_3-ZnO-Na_2O-CaO Glasses

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Abstract:

This study focuses on determining any structural changes that occur in a series of bioactive glasses in which Zinc (Zn) has been incrementally replaced by Gallium (Ga). Structural analysis was conducted using Differential Thermal Analysis (DTA), which yielded a thermal profile of each glass. Also included in the study was whether or not the incorporation of Ga affects the formation of a calcium phosphate layer on the glass surfaces after being submerged in simulated body fluid (SBF). These glasses included Ga because of its antibacterial properties and anti-cancer abilities *in vivo*[1,2].

I. INTRODUCTION

Gallium is being investigated in order to determine its structural role in bioglasses. Gallium serves many potential applications in the field of biomaterials due to its antibacterial properties, its "physiological function related to bone matrix," and use in cancer treatments and therapeutics[34]. A bioactive material is a material that elicits a specific biological response at the interface of the material resulting in the formation of a bond between the tissues and the material.

Glass based biomaterials are playing an increasing role in orthopedics and reconstructive surgery as they can incorporate ions that have a therapeutic effect in vivo. Bioactive glasses are included in this group of materials. Bioglasses are commonly utilized as bone void fillers and can encourage cell proliferation and differentiation upon implantation into the body.

Gallium is "a semi metallic element that exhibits a dose dependent antiosteoclastic effect by reducing in vitro osteoclastic resorption, differentiation, and formation without negatively affecting osteoblasts[5]." A bioactive material is a "material that elicits a specific biological response at the interface of the material resulting in the formation of a bond between the tissues and the material." Consequently, gallium should be further used to promote "interactions with cellular processes and biologically important proteins[6]." Certain gallium compounds have been developed as diagnostic and therapeutic agents especially in the areas of bone, cancer, and infectious disease[6].

A. Previous Studies

Previous studies incorporating gallium into bioglasses revealed gallium's antimicrobial properties as well as its impact on the bioglass's durability[7,8]. Mirco Franchini and others performed an experiment regarding the in vitro bioactivity of gallium-containing phospho-silicate glasses. Franchini and company recognized Ga^{3+}'s antimicrobial properties because of its ability to replace Fe^{3+} in proteins. Previous studies have indicated gallium's antibacterial activity toward staphylococcus aureus[5]. Gallium was also found to have low toxicity which enabled it to be FDA approved for the treatment of calcium-related cancer hypercalcemia. In Franchini's experiment gallium incorporated into phosphosilicate bioactive glasses were analyzed in order to see the impact of the bond between bone and living tissue. Phosphosilicate glasses compared to phosphate glasses deliver metal ions for a longer time in a nearly regular manner due to the higher chemical durability. The silicate network is much stronger due to its covalent character and the covalent bond energy of Si-O. Incorporating gallium into the network of Na-Ca-Phosphosilicate glass is supposed to have a similar effect to that of Al^{3+}. That being said, Ga^{3+} was expected to adopt octahedral and tetrahedral coordination geometry with respect to the oxygen atom. In Franchini's experiment, solid state investigation was performed on four samples: control (0% Gallium), 1.0 molar percent Ga, 1.6 molar percent Ga, and 3.5 molar percent Ga. The samples were analyzed before and after SBF soaking for 1, 4, 15, and 30 days to evaluate the apatite layer formation. The experiment enabled the glasses to be classified in terms of apatite formation rate and Ga^{3+} release. Experimental results proved that increasing the gallium content shifts the role of gallium

from a network former to a network modifier. As a result, gallium incorporated phospho-silicate glasses can be deemed bioactive with an additional antimicrobial effect[6].

Another study has identified gallium as a beneficial substitute into mesoporous bioactive glasses. Apart from its antibacterial properties, gallium also plays a vital role in the normal physiological function related to bone metabolism. Gallium can enhance the properties of the skeletal system because it protects the hydroxyapatite matrix[3]. Gallium stimulates bone formation and improves the mechanical properties of bone. A.J. Salinas and others performed an experiment to see if incorporating gallium into mesoporous bioactive glass would cause the glass to exhibit mesopore order, good textural properties (surface area/porosity), and a quick in vitro bioactive response. Based on Salinas' work, the inclusion of gallium decreased textural properties, but not enough to disturb its use in clinical applications. Therefore, Salinas found that incorporating 3.5% (mol. %) into ordered mesoporous glasses made the glass a promising candidate for bone tissue engineering.

E. Verron, J.M. Bouler, and J. Guicheux have also performed experiments incorporating gallium into biomaterials. They have found that gallium has been shown to substitute calcium in biological apatite. Furthermore, they believed that gallium could be incorporated into calcium phosphate biomaterials by Ca to Ga exchange. Gallium has a high affinity to hydroxyapatite. Due to this affinity, gallium was found to preferentially fix onto bone tissue once it is released from calcium phosphate[5]. Verron, Bouler, and Guicheux concluded that gallium is a potential agent to be associated with calcium phosphate in order to propose an innovative biomaterial with anti-resorption activity.

They found that as gallium content increases, more calcium ions are being replaced by gallium. Consequently, the mechanical properties of biological apatite are improved.

II. METHODS

A. Synthesis

Three glasses were analyzed in this study including one Ga-free glass (*Control*) that was used as the control and two Ga-containing glasses (*TGa-1*, *TGa-2*) which included incremental increases of Ga_2O_3 at the expense of ZnO. Table I lists the glass compositions that were used.

Table I. Glass Compositions (Mole Fraction).

	Control	**TGa-1**	**TGa-2**
SiO_2	0.42	0.42	0.42
Ga_2O_3	0.00	0.08	0.16
ZnO	0.40	0.32	0.24
Na_2O	0.10	0.10	0.10
CaO	0.08	0.08	0.08

B. X-Ray Diffraction

First, x-ray diffraction was used in order to prove each sample is amorphous. XRD data was collected using 40 kV, 30 mA, a step size of 0.05, and a 3 second time/step for the range of 0-80° 2Θ with a Siemens D5000 detector and a copper source.

C. Sample Preparation

To obtain flat glass plates for SBF studies, the powdered mixes of analytical grade reagents were fired (1500°C, 1h) in platinum crucibles and poured into graphite molds. After cooling, the glass was then removed from the molds and annealed at their respective glass transition temperatures. These glass bars were then polished to obtain flat surfaces and cut into equally sized rectangular plates.

D. Differential Thermal Analysis (DTA)

A SDT 2960 Simultaneous DSC-TGA was used to determine the glass transition temperature of the three glass samples with a heating rate of 20°C/minute measured between room temperature to 1300°C.

E. Simulated Body Fluid Preparation (SBF)

SBF was prepared following Kokubo *et al* procedure ensuring that no precipitation occurred[9]. Samples were then taken out of SBF and analyzed after 1, 7, and 14 days. The volume of SBF (*Vs*) used was calculated using:

Vs = Sa/10 (Sa = surface area).

F. Scanning Electron Microscopy (SEM), Energy Dispersive X-Ray Spectroscopy (EDS), and Quantitative Analysis

A Quanta 200F Environmental Scanning Electron Microscope was used to image the samples under a vacuum at a pressure of 0.90 torr. The electron beam was used at a voltage of 20 kV and a spot size of 4.0.

G. Laser Profilometer

A Solarius Laser Profilometer was used to image the glass surfaces at a scan rate of 200 Hz, index of refraction of 1.5, and resolution of 5x5mm.

III. RESULTS AND DISCUSSION

A. Powder Analysis

X-ray diffraction was first performed on each of the three samples to prove that each sample was amorphous. Figure 1 shows the XRD patterns for the respective sample. Each pattern has an amorphous hump, thus proving they are amorphous. SEM images for each sample can be found in Figure 2. These images found in Figure 2 are a compilation of secondary electron and backscattered electron modes.

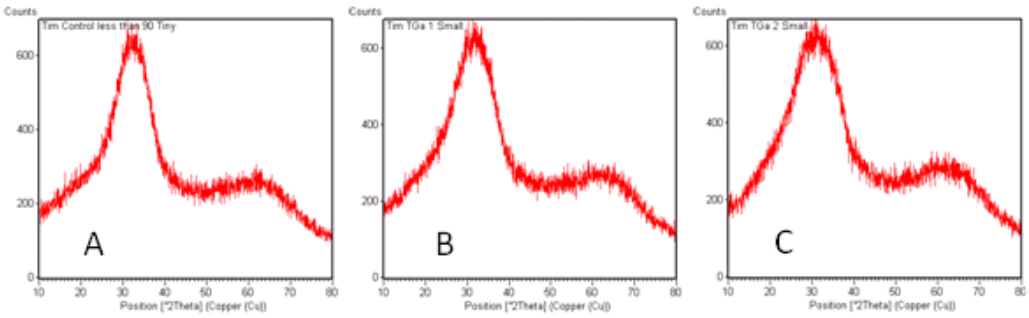

Figure 9. XRD patterns for the three powder samples (A-Control, B-TGa-1, C-TGa-2).

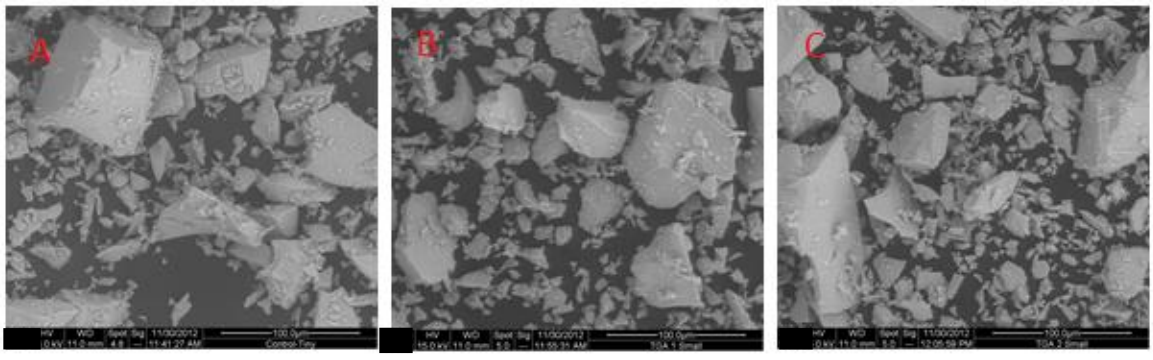

Figure 10. SEM images for three powder samples (A- Control, B-TGa-1, C-TGa-2).

Figures 3-5 show the EDS spectrum for each of the powders. Tables II-IV list the elements found in each powder. These tables highlight the increase of Ga content at the expense of Zn for the series of glasses.

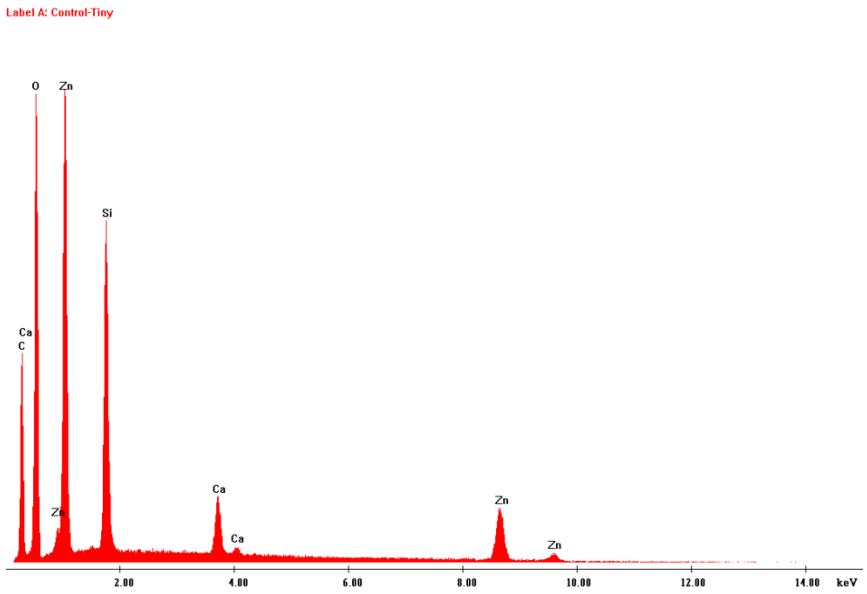

Figure 11. EDS for Control Powder.

Table II. Quantitative Analysis for Control Powder.

Element	Weight %	Atomic %
Oxygen	27.62	53.87
Silicon	16.04	17.83
Calcium	4.66	3.63
Zinc	51.68	24.67

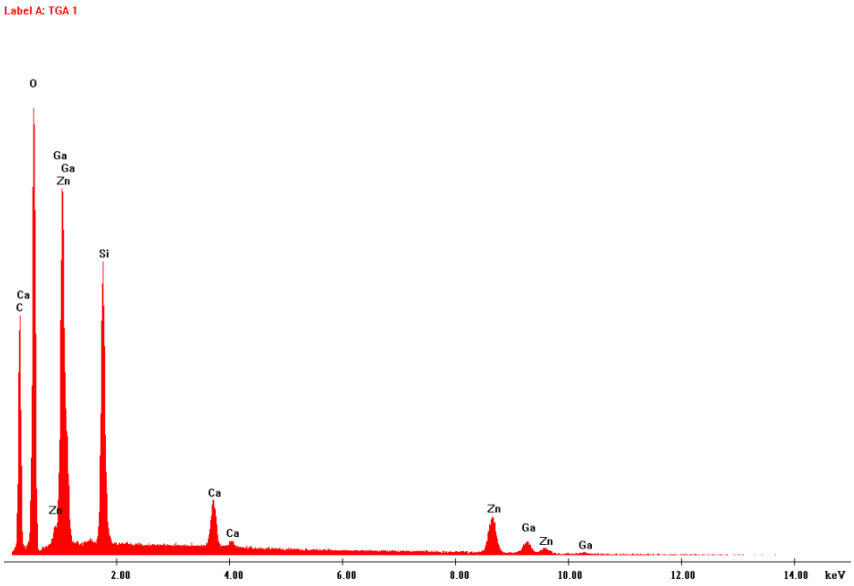

Figure 12. EDS Spectrum for TGa-1 Powder.

Table III. Quantitative Analysis for TGa-1 Powder.

Element	Weight %	Atomic %
Oxygen	27.00	54.33
Silicon	13.93	15.96
Calcium	3.90	3.13
Zinc	36.04	17.75
Gallium	19.13	8.83

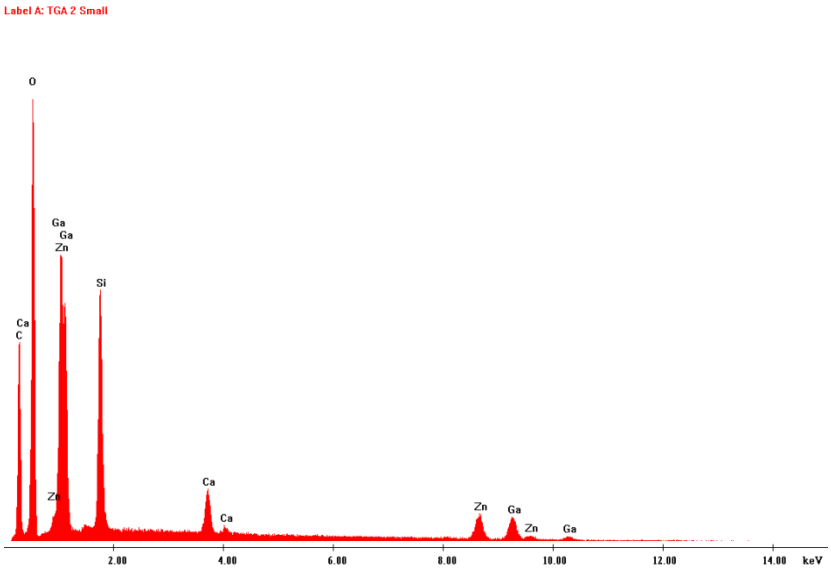

Figure 13. EDS Spectrum for TGa-2 Powder.

Table IV. Quantitative Analysis for TGa-2 Powder.

Element	Weight %	Atomic %
Oxygen	26.47	54.52
Silicon	12.46	14.63
Calcium	3.53	2.90
Zinc	23.66	11.93
Gallium	33.88	16.02

Figures 6-13 and Tables V-VIII include SEM images, EDS spectra, and quantitative analysis for the TGa-1 and TGa-2 glasses after one and 14 days of immersion. Figures 6, 8, 10, and 12 are SEM images and one can visibly see the crystal formations on each of the glass samples.

B. Glass Analyses

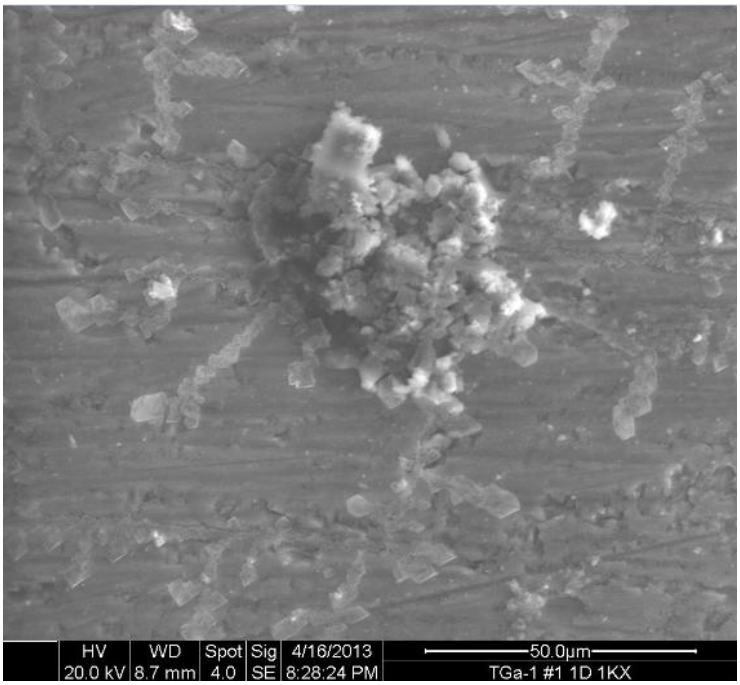

Figure 14. SEM Image of TGa-1 after 1 day immersion in SBF with original magnification of 1000x.

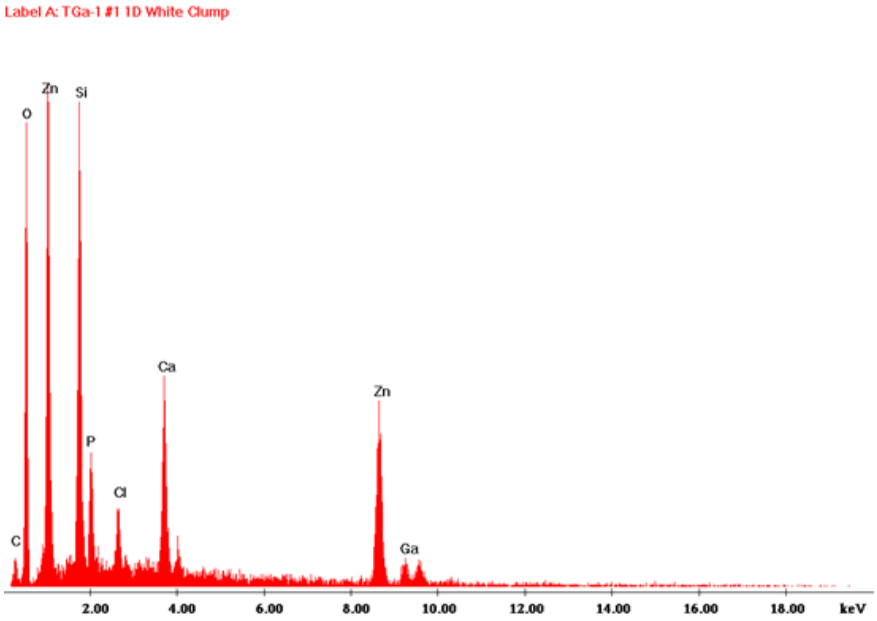

Figure 15. EDS Spectrum for TGa-1 after 1 day immersion in SBF.

Table V. Quantitative Analysis for TGa-1 Glass after 1 day immersion in SBF.

Element	Weight %	Atomic %
Oxygen	25.98	43.74
Silicon	12.78	12.26
Calcium	6.20	4.17
Zinc	34.86	14.36
Gallium	6.49	2.51

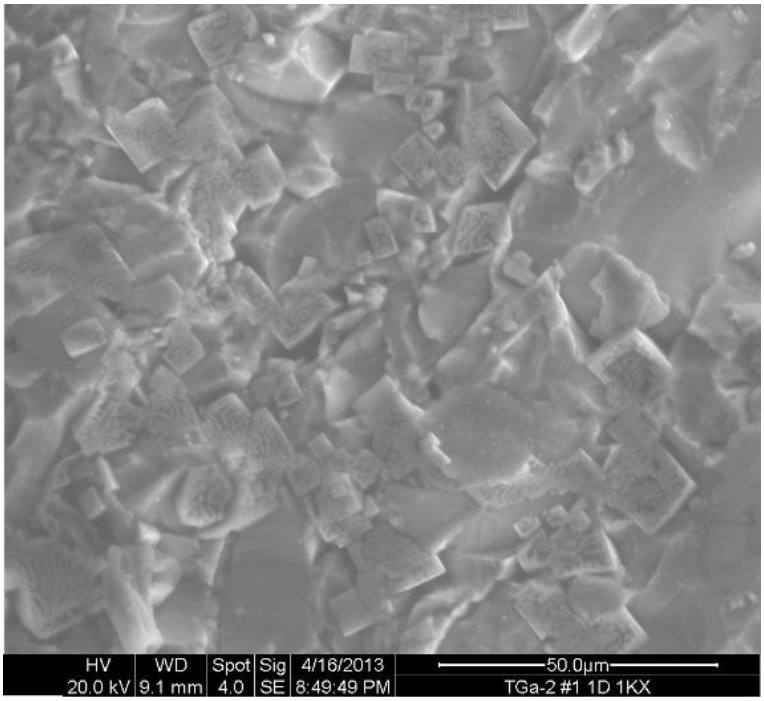

Figure 16. SEM Image of TGa-2 Glass after 1 day immersion in SBF with original magnification of 1000x.

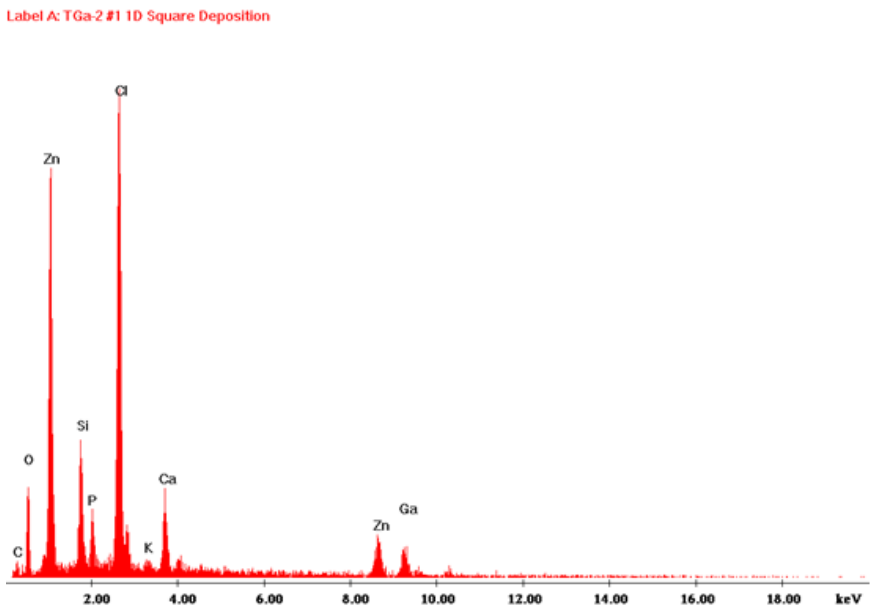

Figure 17. EDS Spectrum for TGa-2 after 1 day immersion in SBF.

Table VI. Quantitative Analysis for TGa-2 Glass after 1 day immersion in SBF.

Element	Weight %	Atomic %
Oxygen	15.17	26.96
Silicon	6.74	6.83
Calcium	5.18	3.67
Zinc	16.49	7.17
Gallium	16.79	6.85

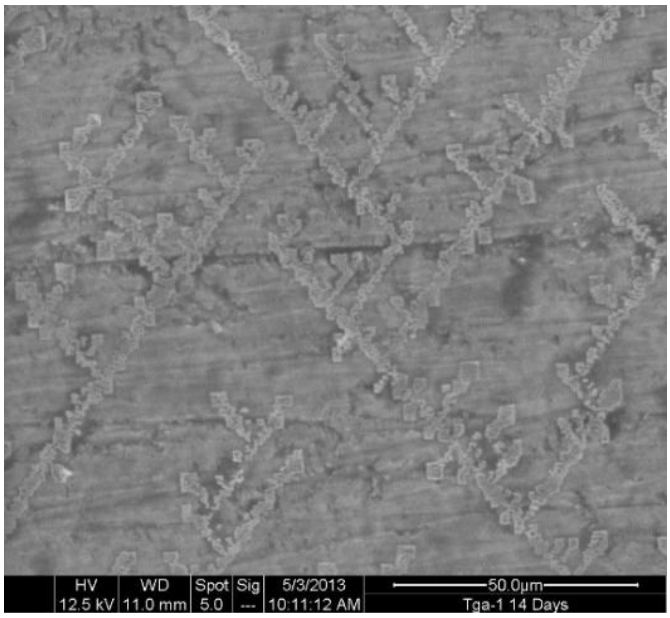

Figure 18. SEM Image of TGa-1 after 14 days of immersion in SBF with original magnification of 1000x.

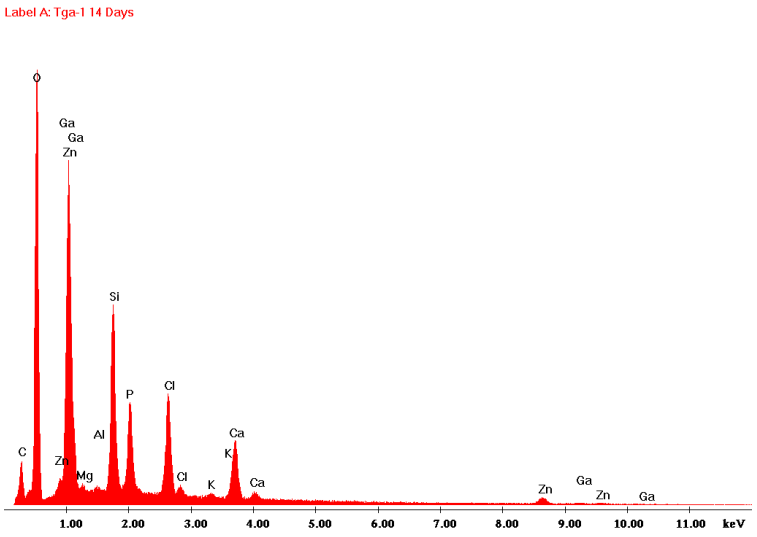

Figure 19. EDS Spectrum for TGa-1 Glass after 14 days of immersion in SBF.

Table VII. Quantitative Analysis for TGa-1 Glass after 14 days of immersion in SBF.

Element	Weight %	Atomic %
Oxygen	60.31	76.58
Silicon	11.71	8.47
Calcium	6.14	3.11
Zinc	4.43	1.38
Gallium	1.06	0.31

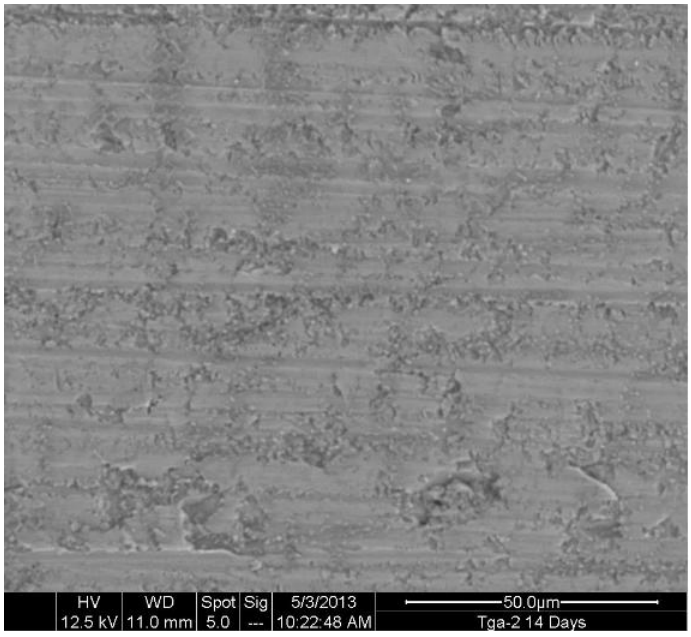

Figure 20. SEM Image of TGA-2 Glass after 14 days of immersion in SBF with original magnification of 1000x.

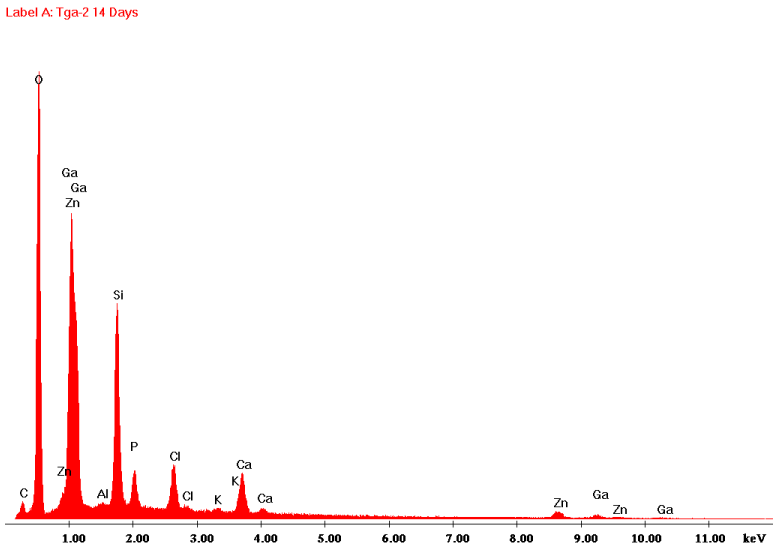

Figure 21. EDS Spectrum for TGa-2 Glass after 14 days of immersion in SBF.

Table VIII. Quantitative Analysis of TGa-2 Glass after 14 days of immersion in SBF.

Element	Weight %	Atomic %
Oxygen	62.60	78.92
Silicon	15.17	10.90
Calcium	4.67	2.35
Zinc	5.41	1.67
Gallium	3.74	1.08

The SEM and EDS results for the TGa-1 and TGa-2 glasses show that Ga concentration in each glass decreased with increasing time spent in the SBF. TGa-1 decreased from 6.49 weight percent Ga after one day of immersion to 1.06 weight percent Ga after 14 days of immersion. TGa-2 also experienced a decrease in Ga concentration. TGa-2 decreased from 16.79 weight percent Ga after one day of immersion to 3.74 weight percent Ga after 14 days of immersion in SBF. The Ga reduction in TGa-2 was more noticeable since this glass had double the mole fraction of Ga as the TGa-1 glass.

The reduction of Ga in the glasses may be a result of Ga acting as a network modifier[10]. If Ga assumes a network modifying role it will be released from the glass into the aqueous environment.

The partial dissolution of the glass particles surface results in the formation of a silica-rich gel layer and subsequently precipitation of a calcium phosphate layer[10]. Tables V and VII show that the Silicon (Si) concentration in the TGa-1 glass decreased from 12.78 to 11.71 weight percent as a result of being immersed in SBF for 14 days instead of just one day. This trend was not seen in the TGa-2 glass, but Si concentration could've increased if the glass samples were allowed to be immersed for a period greater than 14 days. Nonetheless, the TGa-1 sample is more likely to be bioactive because the higher rate of silica dissolution further increases bioactivity[10]. Si content increased from 6.74 to 15.17 weight percent in the TGa-2 glasses (Tables VI and VIII). This result is signficant because an increase in Si concentration means that Silica concentration would've increased. If the concentration of Silica increases, equal molar concentrations of Sodium Oxide and Calcium Oxide were found as well. This is important because if apatite can form on the surface of a material in SBF, one can predict the degree of *in vivo* bone bioactivity[9]. Therefore, TGa-1 may be more bioactive due to the decrease in Si content and TGa-2 may be bioactive because it aids in apatite formation.

C. **DTA Results**

DTA was performed in order to determine the glass transition temperatures of each of the glasses. DTA results were also used in order to detect any changes in the T_g due to Ga concentration. A shift in T_g can indicate that structural changes in the glass are

occurring due to increases in Ga concentration[10]. Figure 14 plots the respective glass transition temperatures, crystalline temperatures, and melting temperatures of the three glasses. Table IX lists these respective temperatures.

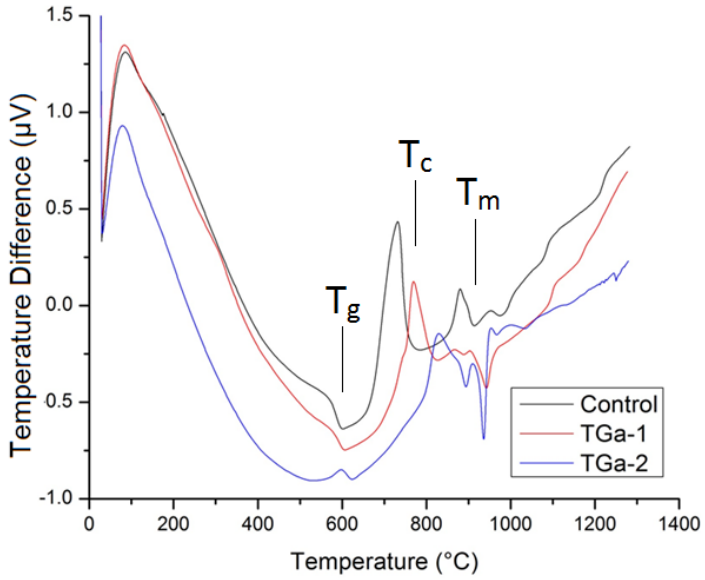

Figure 22. DTA of all three glasses.

Table IX. Glass Transition Temperature (T_g), Crystalline Temperature (T_c), and Melting Temperatures (T_m) for each of the three glasses all in °C.

	T_g	T_c	T_m
Control	586	732	879
TGa-1	597	774	947
TGa-2	614	832	938

Table IX shows that T_g increased as Ga concentration increased. This shift in T_g suggests increased glass stability which may have occurred due to the formation of bridging oxygen groups. It has been suggested that Ga ats as a network former[10]. Bioactive elements included in network forming roles can play an essential role where their incorporation can further control the glass degradation rate and ion exchange process[10]. In this glass series, Ga predominantly acts as a network former; however, Ga may adopt a

newtork modifying role above a certain threshold level. If Ga assumes a network modifying role, it will be released into an aqueous environment which may then provide a therapeutic benefit[10]. Consequently, DTA results can be used to find the T_g of each glass as well as identify trends in T_g data as a result of glass composition.

D. Laser Profilometry Results

Figures 15-18 are sample surface roughness scans for the TGa-1 and TGa-2 samples after one and seven days of immersion. Figure 19 is a sample surface roughness scan of TGa-2 after 14 days of immersion. TGa-1's profilometry scan after 14 days of immersion had too many defects to produce a useable surface roughness scan.

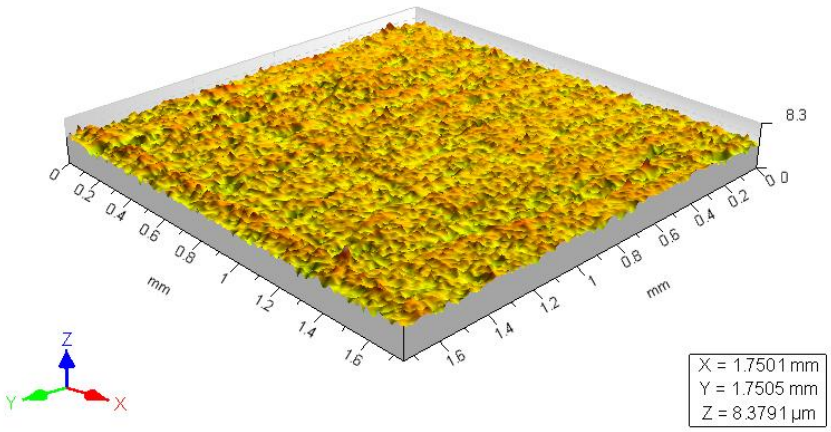

Figure 23. Profilometer surface roughness of TGa-1 Glass (1 Day) with 40% level of detail and 10% height amplification.

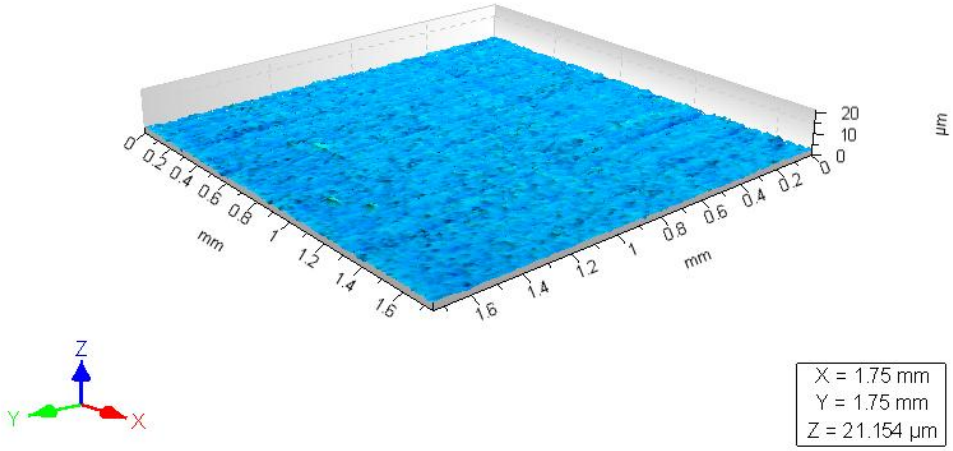

Figure 24. Profilometer surface roughness of TGa-1 Glass (7 Days) with 40% level of detail and 10% height amplification.

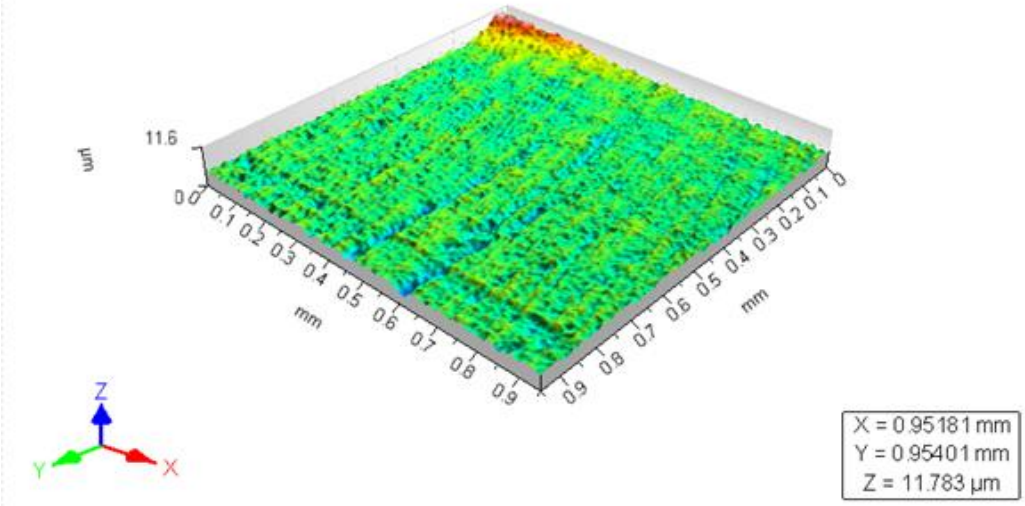

Figure 25. Profilometer surface roughness of TGa-2 Glass (1 Day) with 40% level of detail and 10% height amplification.

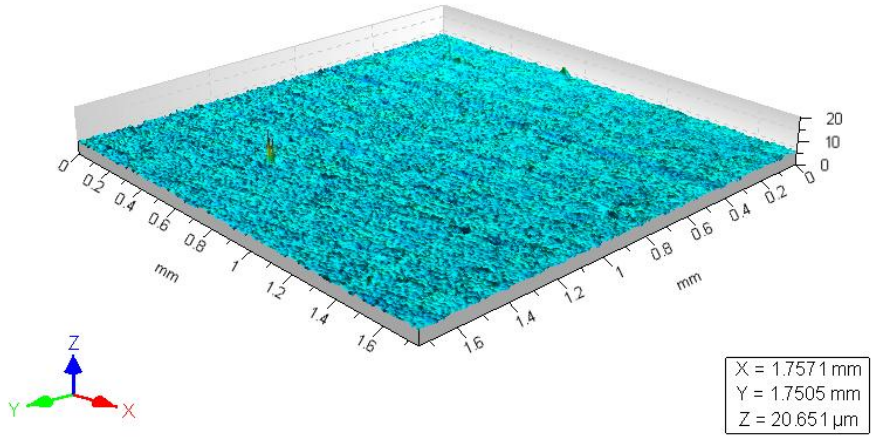

Figure 26. Profilometer surface roughness of TGa-2 Glass (7 Days) with 40% level of detail and 10% height amplification.

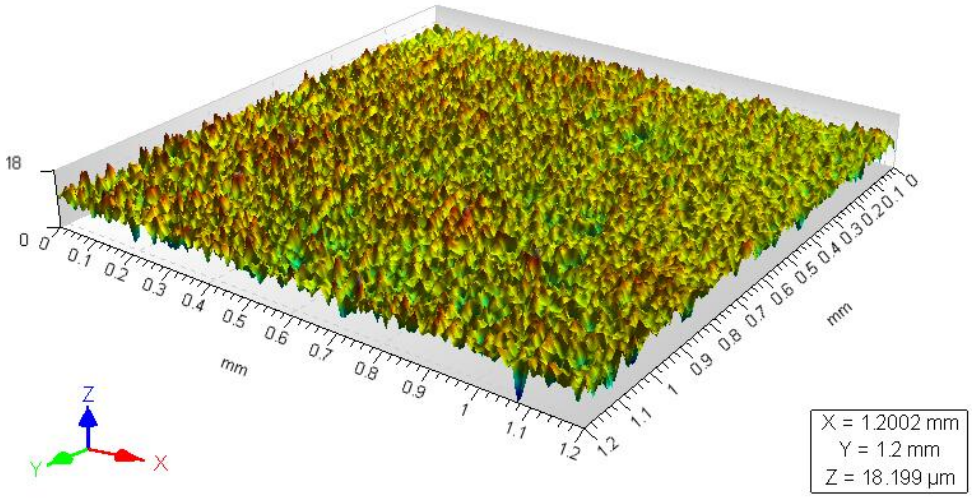

Figure 27. Profilometer surface roughness of TGa-2 Glass (14 Days) with 40% level of detail and 10% height amplification.

The figures above show that all samples showed varying degrees of surface roughness. Table X lists the average mean heights for the profilometry images (Figures 15-19).

Table X. Mean height (μm) for surface roughness scans (Figures 15-19).

Sample	Mean Height (μm)
TGa-1 (1 Day)	0.39055
TGa-1 (7 Days)	0.37223
TGa-2 (1 Day)	2.7101
TGa-2 (7 Days)	0.36444
TGa-2 (14 Days)	1.4213

From Table X, it is hard to establish a trend in the surface roughness data. The mean heights of the roughness scans do not follow a linear trend. If TGa-2 (1 Day) is ignored from the TGa-2 glasses, then the surface roughness would have nearly tripled between a 7 day immersion period and 14 day immersion period for the TGa-2 glasses. However, TGa-1 samples show a decrease in mean height as immersion time increased. Therefore, the profilometry scans did not provide a trend in mean height.

Glass dissolution may be controlled by understanding the conditions in which ions assume different coordination states. Depending on the coordination states of Ga and other elements of the glass series being investigated, the release rate of ions may also be altered[10]. The release of these ions and the amount of glass dissolution will impact surface roughness. Consequently, laser profilometry scans should be different for each sample based on coordination states due to the molar concentrations of the various elements in each glass.

IV. CONCLUSIONS

Overall, this study investigated how the surface of three bioactive glasses changed by incorporating more Ga at the expense of Zn. Together SEM images and quantitative analysis were able to identify elements present on the surfaces of the glasses. The quantitative analyses from Tables V and VII show that Si content decreased for the TGa-1 glass the longer it was submerged in SBF. This result is significant because the higher rate of silica dissolution increases bioactivity. Quantitative analyses from Tables VI and VIII highlight the decrease in Si concentration for TGa-2 the longer it was kept in SBF. This proves significant because apatite formation may occur more readily. The ability to form apatite on the surface enables the prediction of *in vivo* bone bioactivity of the bioglass.

Laser profilometry images also proved that all of the glass surfaces had a degree of surface roughness; however, no linear trend was found in the mean height of the samples' surface roughness. Because glass dissolution depends on the coordination states of ions and the release rate of these ions, it seems that sample roughness should follow some sort of trend for each particular sample.

Crystals had formed on the surface of every glass even after just one day of immersion in SBF. The precipitation and dissolution of the glass surfaces is noteworthy because of their effects on bioactivity for this series of bioglasses. In the end, the sample surfaces of the glasses did change structurally due to the incorporation of Ga as well as immersion time in SBF.

V. SUGGESTIONS FOR FUTURE WORK

Future works related to this study would require more glass samples. For the present experiment there were only two samples for the control and TGa-1 glasses that were study after each incubation period. The TGa-2 glasses only had one sample that could be analyzed after each incubation period. The increase in number of samples will enable a better compilation of data and consequently improve analyses.

Beyond these sample limitations, several other experiments could be performed including: annealing samples of each glass 20°C higher than their glass transition temperatures (T_g), Atomic Force Microscopy (AFM), cross polarization, elemental analysis of the ions released into the simulated body fluid, and solubility testing. Also, more experiments should be performed in order to test how well the bioglass reacts with bone.

A. Annealing Above the T_g

One of the first experiments that should be performed would be to anneal each glass 20°C above its respective T_g that was determined using Differential Thermal Analysis (DTA). This experiment would eliminate the polishing process because the surface of the glasses would already be smooth. Annealing several degrees above the glass transition temperature would not introduce any unnecessary stresses due to polishing of the glass surface.

B. Atomic Force Microscopy (AFM)

AFM could also be utilized on the samples that were annealed above their glass transition temperatures in order to get the most accurate surface analysis profile. The

glasses should be scanned prior to SBF immersion and afterwards. Therefore, accurate surface scans can be compared to before and after precipitation. AFM should be used on samples annealed above the glass transition temperature because the high resolution scans are extremely surface sensitive. Samples that were polished may not reflect an accurate surface due to defects.

C. Cross Polarization

Cross polarization may also be used for future analyses too. Similar to the AFM experiments, cross polarization experiments should also be taken before and after SBF immersion. Cross polarization will be able to identify any stresses present before immersion and how these stresses may have changed as a result of SBF immersion times. Cross polarization can be done on samples that were annealed at the T_g and above the T_g to compare the differences in stresses between polished and unpolished samples as well.

D. Elemental Analysis

Various surface analyses can be performed on each of the glasses. The quantitative analysis in Tables V-VIII can be used to compare the amount of each element in the glass after being immersed in the SBF for the respective number of days. Elemental analysis should also be used to determine what ions were released into the SBF after the glasses were immersed.

VI. REFERENCES

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