The effect of titanium dioxide on the structure and bioactivity of B_2O_3 –P_2O_5 –Na_2O –CaO glasses

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Abstract Glass is an amorphous solid defined as a rigid material whose structure lacks crystalline periodicity. The pattern of amorphous atoms and/or molecules is not repeated periodically in three dimensions. If glass is soaked in a physiological solution as a simulated body fluid (SBF) and when hydroxyapatite (HA) appears in XRD diagram and in SEM analyses the glass is called bioactive, such as silicate glasses, borosilicate glasses, phospho-borate glasses. In this work it is intended to control the rate of dissolution and glass bioactivity By substituting P_2O_5 with TiO_2 progressively in the bioactive Phospho- borate glass of basic composition $0.07P_2O_5$ – 0.46 B_2O_3 - 0.24 CaO – 0.23 Na_2O and TiO_2.To prepare this composition which characterized by its bone-bonding ability. The system was studied using density measurements and differential thermal analysis (DTA). The results showed an increase in density and a decrease in molar volume, which indicates creating non bridging oxygen (NBO) and TiO_2 acts as a modifier in a borate glass network. A Glass bioactivity study has been done on the different prepared samples by immersing it in (SBF) solution for prolonged times (near 30 days) during which weight loss with pH measurements were performed at specific intervals of time.
The results showed a decrease in pH and weight loss with increasing the TiO_2 content which act as a nucleating agent. The XRD and SEM analysis of glass after immersed in SBF solution emphasize the formation of a crystalline HA on the surface of the samples, which indicates a bioactivity of glass which can be used in the field of bone repairing and various clinical applications. IR spectral studies on post and pre immersed samples has been carried out as well. The results showed that BO_3 is converted to BO_4 in the borate glass structure which assures that TiO_2 act as a modifier. Through substituting P_2O_5 by TiO_2 in the glass system, a decrease in TiO_2 content in the glass will increase P_2O_5 and hence increase HA which indicates increase the glass bioactivity and vice versa in case of increasing TiO_2 content. This result was assured by the IR spectra obtained.

Index Terms— phosphor borate glasses; Bioactivity; HA layer.

1 INTRODUCTION

Bioactive glasses are widely investigated in the field of medical applications. They able to form direct strong bonds with the living bone without the formation of surrounding fibrous tissue. [1] For their unique properties they are used as materials for bone substitution.
Nowadays, bioactive glasses are used for reconstructing damaged bones or tissue. Also, they are used in repairing the diseased bones and tissues. [2] As scaffold materials, they have various appealing properties, for example their ability to be converted to hydroxyapatite (HA) in vivo. In HA Calcium to phosphate ratio within bone is approximately 1.67 [3]. The bioactive glasses also have a high ability to bond firmly to hard and soft tissues.[4,5]. Silicate bioactive glasses, such as 45S5 glass (containing 45 % of SiO_2 with Na_2O, CaO, P_2O_5 as remaining constituents) and compositions based on 45S5, such as 13-93 (20 CaO, 53 SiO_2, 12 K_2O, 6 Na_2O, 5 MgO, 4 P_2O_5wt%) and S53P4 (53 SiO2, 23 Na_2O, 20 CaO and 4P_2O_5mol%), have been widely investigated [4]. Some borate-based glasses have been found to be bioactive in literatures [6,7]. Scaffolds of borate bioactive glass designated 13 - 93B3 (56.6 B_2O_3 18.5 CaO, 11.1 K_2O, 5.5 Na_2O, 4.6 MgO, 3.7 P_2O_5, wt%) , a composition designed where SiO_2 is replaced with B_2O_3, has been found to be converted faster to HA and to have high ability to support faster bone growth in rat calvarial defects comparing with scaffolds of silicate glass. [8] However, the effect of the microstructure of borate 13 - 93B3 scaffolds on tissue ingrowth has not been studied yet. These glasses, when exposed to physiological Solutions or simulated body fluid (SBF) which is a solution prepared in the laboratory and have ionic concentration similar to human plasma or calcium phosphate solutions [9]. An amorphous calcium phosphate layer is formed on their surfaces, this layer may be crystallizes to form biologically active hydroxyl carbonate apatite layer (HA) within a few days. This phase is responsible for the interfacial bonding. It is chemically and structurally equivalent to the mineral phase in bone [10]. Borate glasses possess low chemical durability. They convert rapidly to calcium phosphate in physiological media [11]. Recent studies have been conducted on borate glasses found that the hydroxyapatite layer is formed faster than that with silica glass content proposed by Hench [12]. However, the borate based bioglasses shows very good bioactivity both in vitro and in vivo [13]. The degradation rate (i.e. The conversion to HA) has been found to be too rapid to match the growth rate of the new bone. It is considered that, the matching between the rate of degradation and the time of the remolding the bone is very important for biomedical applications. The degradation rate may be controlled by modifying the glass composition, with some metallic oxides in the glass network, for example TiO_2 [14, 15]. Titanium dioxide (TiO_2) is a powder that has a low-solubility. It consists of fine crystals, white, and odorless. It is considered to exhibit relatively low toxicity [16,17]. It has good properties, such as good resistance to corrosion, high fatigue strength, whitening, machinability, biocompatibility photo catalysis, electrical properties, and optical performance [18]. TiO_2 adsorbs water at the surface, forming Ti^+OH groups. Such groups induce apatite nucleation and crystallization in SBF [19]. The previous studies on bioactive boro phosphate glasses with added alkaline earth oxides such as Na_2O, CaO and the TiO_2 effects on the bioactivity of glasses showed that:

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Some researchers have studied B_2O_3–SiO_2–Na_2O–CaO glasses mixed with different concentrations of TiO_2 indicated that about 6.0 mole% of TiO_2 (octahedral titanium ions), is the optimal concentration for the better bioactivity of these glasses [20]. In other studies the glass in the system CaO–P_2O_5–B_2O_3 have been studied by μ-Raman and FT-IR spectroscopies, and they found That the glass network is commanded by highly charged species from phosphate tetrahedra with 3 (Pyro) or 4 (ortho) NBOs The boron atoms are based in three coordinated sites in the form of BØ2O ⁻ units in this glass and it has a catalytic effect of favoring bioactivity after the glass was soaking in SBF solution within a few days [21]. Also in the study of the glass system $0.6B_2O_3$, $0.2Na_2O$, 0.2CaO and SrO gradually substituting CaO, they found that the appearance of characteristic IR absorbance peaks in the range 550–680 cm^{-1} confirming the presence of HA, The corrosion behavior of the glasses and glass-ceramics indicate the increase of weight loss with the increase of SrO content.[22].The aim of the present work is to study the role of TiO_2, which successively replaces P_2O_5 in ternary soda lime borophosphate glass, in order to control its bioactivity and rate of dissolution The present study includes detailed structural FTIR (Fourier transform infrared) investigations of the prepared glasses before and after being immersed in SBF solution, X-ray analysis of the crystalline species separated after immersion in the SBF solution and also scanning electron microscope studies (SEM) which were performed to follow up the change in morphology of the glass serface after immersion in SBF solution and to investigate both its degradation behavior and biocompatibility.

2 EXPERIMENTAL DETAILS:

2.1. Preparation of glasses

Glass samples were prepared using chemically pure B_2O_3, CaO, Na_2O,P_2O_5 and TiO_2 which taken in mol%.The batches were weighted and melted in porcelain crucibles at 1220°C for 2 hours. The melting was stirred well several times to achieve homogeneity and it was poured into a brass moulds and immediately put into a muffle furnace regulated at 400 °C for annealing purpose. After that it was left to cool to reach room temperature at a cooling rate of about 20 °C/h.

2.2. Density measurements

The densities of the glass samples have been measured by the standard Archimedes' principle method using toluene as buoyant liquid to an accuracy of $0.001 g/cm^3$ with digital balance (Shimadzu make AUY 220 Model). The density ρ_{exp} is given by the eqation

$$\rho_{exp} = \frac{W_a \rho_t}{(W_a - W_b)} \quad (1)$$

Where W_a is the weight of the glass sample in air, W_b is the weight of the glass sample in the buoyant liquid, (W_a-W_b) is the buoyancy, ρt is the density of buoyant (toluene). The molar volume V_m was calculated from the formula

$$V_m = \frac{\sum n_i M_i}{D} \quad (2)$$

Where Mi is the relative molecular mass of the component i and ni are its molar fraction.The additive oxide volume, V_o for each glass composition is calculated using the relation:

$$V_o = \sum_i \left(\frac{n_i}{d_i} M_i\right) \quad (3)$$

Where di is the density, Mi is the molecular weight and ni is the mol fraction of ith component (crystalline oxide)
Excess volume (or volume deviation), V_x is defined as the difference of V_m and V_o

$$V_x = V_m - V_o \quad (4)$$

The oxygen packing density of the glass samples were calculated by the following relation

$$OPD = 1000 * d * (O)/M \quad (5)$$

Where d is the glass density, (O) is the number of oxygen atoms per formula units and M is the molecular weight of glass [Altaf and Chaudhry (2010)].[23]

2.3. Thermal analysis

Thermal characterization was performed using a Setaram differential thermal analyzer (DTA) ((TA-50) Shmadzu, Japan (1990)) on powdered glass samples to determine the glass transition (Tg), crystallization (Tc) at a heating rate of 20°C min^{-1} up to 800°C

2.4. Preparation of SBF solution

The preparation of SBF soln. Is carried out according to the method proposed by Kokubo et al [24] .Its composition is explained in the table (1). The solution was buffered to (potential of hydrogen) pH = 7.4 with Tris-buffer (hydroxyl methyl amino methane) and hydrochloric acid.

TABLE (1)
Ionic concentration (i.c.) (mM) of (SBF)

SBF	K^+	Mg^{2+}	Na^+	Ca^{2+}	Cl^-	HCO^{3-}	HPO_4^{2-}	SO_4^{-2}
I.C.(mM)	5.0	1.5	142.0	2.5	147.8	4.2	1.0	0.5

2.4. X-ray diffraction analysis

X-ray diffraction technique was used to identify the crystalline phases formed within the samples before and after immersion. The X-ray charts were analyzed to identify the structural changes. The samples were ground and the fine powder was examined using (Schimadzu Labx XRD-6000) using CuKαradiation at 40 kV, 2θ between 5° to 90°.

2.5. Solubility test

The degree of solubility of the glass samples was determined by measurements of their weight loss in SBF solution at 36.5 °C. Selected glass specimens of dimensions of acceptable accuracy were ground and polished. The dimensions of the samples were measured and hence they were placed in polyethylene beakers containing certain volumes of the SBF solution. Where, the ratio of the area of the samples to the volume of the solutions was fixed to be 0.075 cm^{-1} to get an accurate comparison [25]. The samples were removed from the solution and excess moisture was cleaned by tissue paper at various time intervals and then reweighed. The glass solubility or corrosion has been determined by measuring the

percent changes of weight loss. Solubility measurements were repeated twice for obtaining accurate weight loss data [24]. Measuring the initial weight (M_o) of each sample and the weight (M_t) at time t, the weight loss per unit area (A) was obtained as follows:

$$\text{Weight loss (gm cm}^{-2}) = \frac{(M_o - M_t)}{A} \quad (6)$$

2.6. pH measurements

When bioactive glasses dissolved in simulated body fluid, changes in solution pH are very important to analyze. pH values are easily measured with a pH-meter. The calibration of the electrode against buffer solution was performed at an interval of 24 h.

2.7. FTIR measurements

Fourier transform infrared (FTIR) absorption spectra of the prepared glass samples were measured at room temperature in the wavenumber range 2000–400 cm^{-1} using an FTIR spectrometer (Mattson5000, USA). Fine powder of the samples was mixed with KBr in the ratio 1:100 for quantitative analysis and the mixture was subjected to a load of 5 tons/cm^2 in an evocable die for 5 min to produce clear homogeneous discs . IR absorption spectra were immediately measured after preparing the discs to avoid moisture attack. The measurements were taken before and after immersion of the samples in SBF solution and were repeated twice to confirm the positions of the IR peaks.

2.8. Scanning Electron Microscopy(SEM)

The microstructure characteristics of the samples were investigated by analytical scanning electron microscope, (JSM 6360).

3 RESULTS

3.1. Chemical composition of the studied glasses.

Table.2 shows the different investigated glass compositions (0.07−x) P_2O_5– 0.46 B_2O_3 - 0.24 CaO – 0.23 Na_2O - xTiO_2, (with x = 0.0; 0.02; 0.04; 0.06 in Mol %), on the TiO_2– B_2O_3–P_2O_5–CaO–Na_2O glasses. The B_2O_3, CaO, Na_2O content is fixed at 46, 24,23 mol% respectively, for samples A,B,C and D where P_2O_5 is gradually replaced by TiO_2 in a molar base.

TABLE (2)

Specifics of the chemical composition of the studied glasses in mol%

sample code	*CaO* mol%	*P_2O_5* mol%	*Na_2O* mol%	*B_2O_3* mol%	*TiO_2* mol%
A	24 %	7 %	23 %	46 %	0 %
B	24 %	5 %	23 %	46 %	2 %
C	24 %	3 %	23 %	46 %	4 %
D	24 %	1 %	23 %	46 %	6 %

3.2. Density analysis of the prepared glasses

The density of the samples, molar volume, additive crystalline oxide volume and volume deviation are measured and presented in the Table 3.

TABLE (3)

Density (d), molar volume (V_m), additive crystalline oxide volume (V_o), excess volume (V_x) and oxygen packing density (OPD) data of B_2O_3–P_2O_5–Na_2O–CaO: TiO_2 glasses for different samples A,B,C and D

Sample code	*d* *g/cm³*	*(V_m)* *cm³mol⁻¹*	*(V_o)* *cm³mol⁻¹*	*(V_x)* *cm³mol⁻¹*	*OPD* *g atom liter⁻¹*
A	2.536	27.43	32.16	- 4.73	80.075
B	2.653	25.8	31.35	- 5.55	82.962
C	2.557	26.28	30.54	- 4.26	79.153
D	2.590	25.46	29.73	- 4.27	79.327

The densities of the samples have been found to increase from 2.54 to 2.59 g/cc as the TiO_2 content in the glass increases except for sample B which has a high density of 2.653 g/cc. It is known that the density of the glass depends on the structural compactness, cross-link density, the change in geometrical configurations, co-ordination number, etc.

3.3. Thermal analysis

The DTA diagram is a plot of heat changes of the glass related to temperature and it is used to determine temperatures at which phase transition occurs.

Figure 1 and table 4 shows the effect of TiO_2 content on three temperatures;

i) The transition temperature, Tg (which is determined as the midpoint of the change in Cp in the region of the glass transition),

ii) The crystallization temperature, Tc, (the onset of the first crystallization peak)

iii) The difference between the crystallization temperature and the transition temperature (ΔT = Tc – Tg). It can be noticed that the increase of TiO_2 content decreases the Tg values except sample B which increase in Tg .

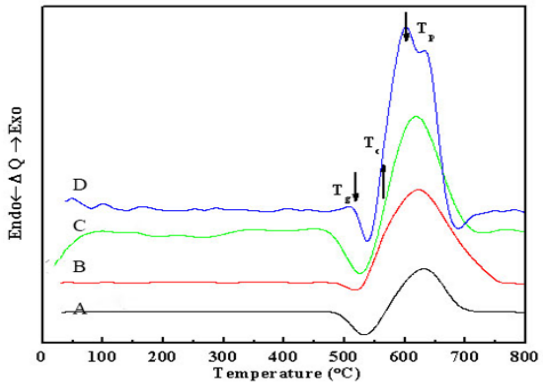


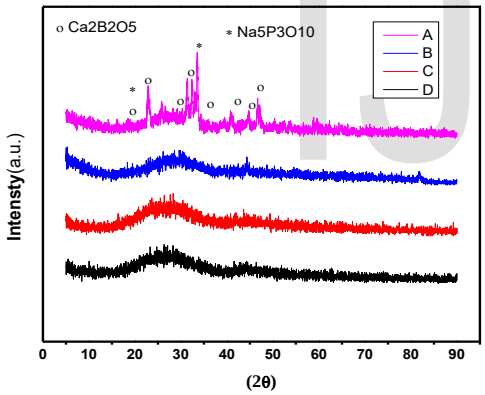
Figure (1): DTA curves of the glass specimens A, B, C and D at a Heating rate 20^0C/min.

TABLE (4)

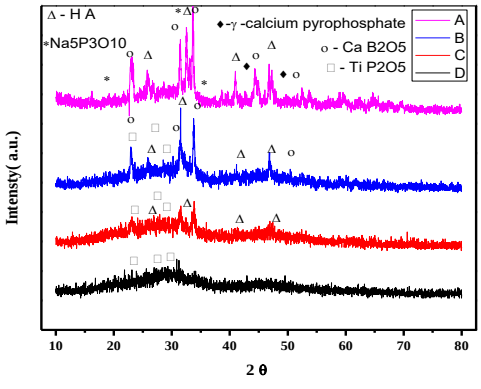
Thermal parameter values of the prepared glasses

sample code	*Tg (°C)*	*Tc (°C)*	*ΔT=Tc-Tg (°C)*
A	491	560	69
B	493	577	84
C	489	540	51
D	477	557	80

3.4. X-ray diffraction (XRD) of the bioactive glasses.



(a)



(b)

Figure (2): XRD patterns of bioactive glass samples A,B,C and D
(a) Before immersing the samples in SBF.
(b) After immersing the samples in SBF for 30 days at 37^oC.

Figure (2a) shows X-ray diffraction patterns of the glass samples before immersion in SBF solution. It is obvious that the following crystalline phases, calcium borate CaB_2O_4 (JCPDS 22-0141 and sodium phosphate oxide $Na_5P_3O_{10}$ (JCPDS 02-0923) which are present as the main constituent in the glass ($0TiO_2$).The other samples are poorly crystallized and nearly constant change in crystallinity by increasing TiO_2 concentrations .In (Fig 2b) XRD patterns of the glasses soaked in SBF for 30 days at 37^oC show increase in intensity of crystalline phases than samples before immersion in SBF solution and a decrease in intensity on adding TiO_2. Also show the appearance of hydroxyapatite phase $Ca_{10}(PO_4)_6(OH)_2$ (JCPDS 72-1243) which emphasis the formation of HA (hydroxyl apatite) on the surfaces of the glass particles . The same diffractograms also exhibited a diffraction peaks due to γ-calcium pyrophosphate phase.

3.5. Solubility testing

Figure (3) shows the dissolution of the glass samples investigated in vitro after immersion in SBF solution for 15 days at 36.5^oC. The weight loss percentage of the (B_2O_3-P_2O_5-Na_2O-CaO) glasses doped with various concentrations of TiO_2 due to immersion in SBF (solution) as a function of dissolution time is also presented in Fig 3.it is to be noted that the degradation has gradually increased with time, but the rate of increasing is fast in sample (A) and slow with increasingTiO_2 concentration, in other words the addition of different concentrations of TiO_2 to the system increase the durability of prepared glass. The dissolution continued until the reaction with SBF is finished by formation of a crystalline hydroxyapatite layer on the surface of bioglass sample.

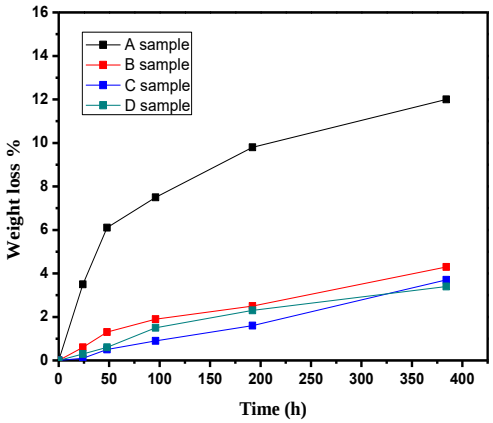


Figure (3): Percentage of weight loss vs dissolution time of B_2O_3-P_2O_5-Na_2O-CaO:TiO_2 glasses during degradation in SBF solution maintained for 15 days at 36.5^oC

3.6. pH measurements

Figure 4 shows the change in pH values from 7.4 to 8.0 of the glass samples after immersing in simulated body fluid (SBF) solution for 1 to 51 days at 36.5°C. The increase of pH of glass samples indicates more alkalinity .The rate of increase the alkalinity in the first 8 days is high and become low after that. After 8 days the slower rate varies according to the increase of TiO_2 concentration. The greater the TiO_2 concentration is the slowest in the rate.

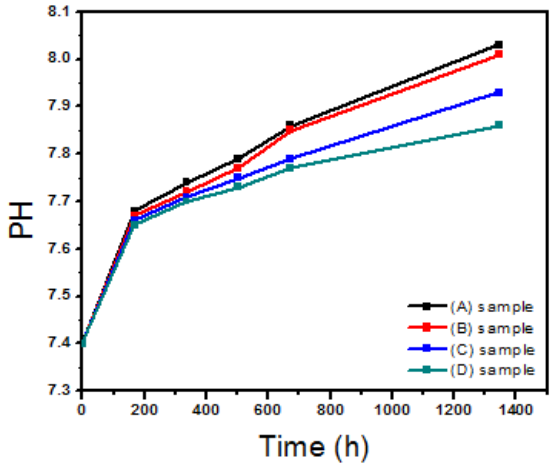


Figure (4): pH changes in SBF after immersion at different periods at 36.5oC of study glass samples A, B, C and D.

3.7. FTIR spectra of bioactive glasses

The structure of Borate glasses B_2O_3 consists of triangular borate (BO_3) units arranged mostly in boroxol groups.

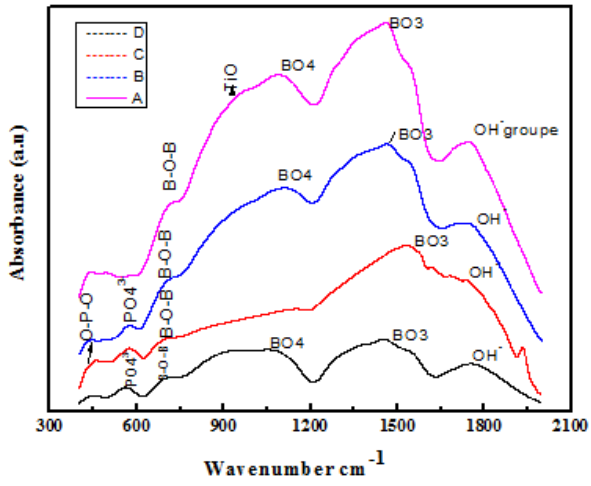
The addition of alkali oxide (e.g.Na_2O, CaO) changes some of the triangular borate units into tetrahedral (BO_4) units, then the formation of a more BO_4 groups stop and the excess modifier oxide forms non-bridging oxygens [20]. The peaks observed in 427–476 cm^{-1} are assumed to be due to vibrations of modifier cations (e.g. Ca^{2+}, Na^{+}) in these glasses [26 , 27].The prepared borate glasses are expected to contain both triangular (BO_3) and tetrahedral (BO_4) units with ratio depends on the composition of glass constituents.

Figure (5a) illustrates the IR spectra of the studied borate glasses before immersion in SBF solution. The strong bands in the range of 1465–1530 cm^{-1} (due to B -O stretching of BO_3 units) can be observed. The absorption band between 900 and 1200 cm^{-1} is also observed, which is due to

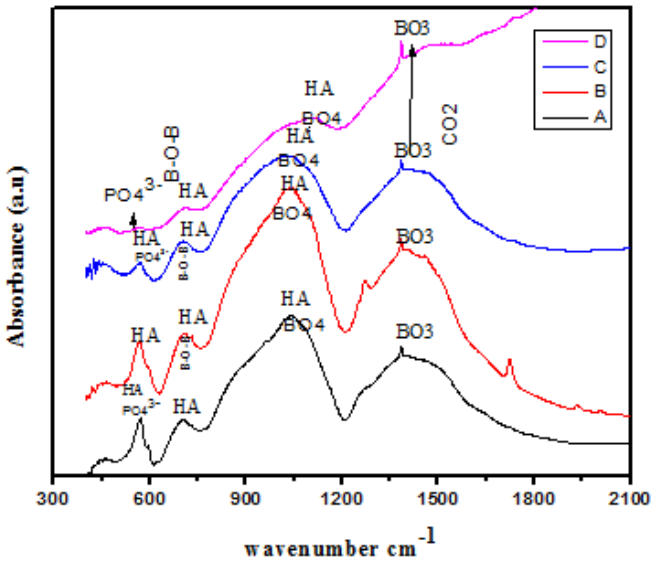
B–O stretching vibration of tetrahedral [BO_4] units.

The spectra exhibited vibrational bands at about 930 cm^{-1}corresponds to a Ti–O band, table (5) ,it appears in rich Ti sample (D). The bands around 700 cm^{-1} is due to bending of B–O–B linkages in the borate network, we note shift from 689 to 705 cm^{-1} by increasing TiO_2 concentration. The peaks observed at 430–460 cm^{-1} are due to vibrations of modifier cations (e.g. Ca^{2+}, Na^{+}) in the glass [22]. The observed absorption band between 560 and 570 cm^{-1} is attributed to υ^{4-} P-O bending vibrations in PO_4^{3-} units. The broad peak at 3450 cm^{-1} is due to symmetric stretching of O–H groups (originated from absorbing water) and absorbed moisture. The IR absorption bands recorded from the sample surface after 30 days immersion in SBF are illustrated in Fig (5b). The decrease of the intensity of the broad band at 1280–1500 cm^{-1} indicates that the phases containing BO_3 are more soluble in the immersed SBF solution than the phases containing BO_4 groups by increasing the modifier (TiO_2) concentrated. Strong vibrational band in the IR spectra of post immersed samples at about 1020- 1045 cm^{-1} can be referred to the superimposition of the vibrational band due to PO_4^{3-} groups with that of BO_4 units in that region [28].The phosphate mode appears at 577 cm^{-1} is assigned to asymmetric amorphous calcium phosphate apatite and the appearance of three peaks at about 560–586 , 708–711 and 1020- 1045 cm^{-1} confirms the formation of calcium phosphate (hydroxyapatite)[HA] layer that formed on the surface of samples [29]and the peak decrease by increasing TiO_2 concentration in the glasses .

The boron bridged phosphate unit peak at 1000 cm^{-1} is diminished; the peaks of the pyrophosphate units are diminished, while the whole spectrum looks like that of hydroxyapatite (spectrum).



(a)



(b)

Figure (5): FT-IR spectra of bioactive glass samples A,B,C and D
(a) Before SBF solution treatment.
(b) After SBF solution treatment for 30 days at 37°C.

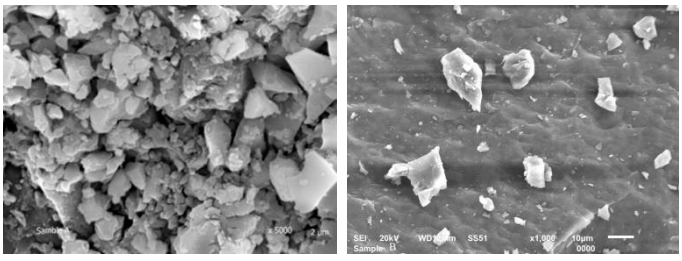
In addition to these bands we can find a band abut 1420 - 1480 cm^{-1} which are attributed due to carbonate groups $[CO_3]^{2-}$ indicating the precipitation of B-type hydroxy carbonate apatite, (HCA) [30].

TABLE (5)
Data on FTIR band positions (in cm^{-1})
of B2O3-P2O5-Na2O-CaO:TiO2 glasses.

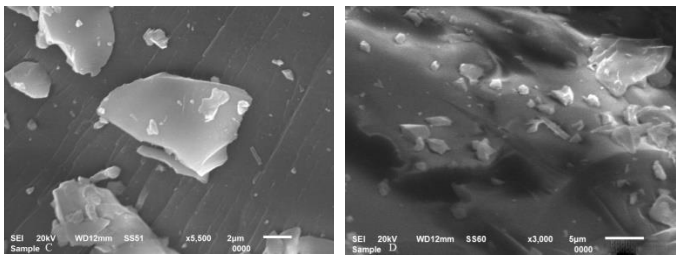
Sample ID	peak bands cm^{-1}	Assignments	References
A ,B ,C,D	550 - 680	Calcium phosphate (hydroxyapatite)	[31]
A	708 – 711	binding vibration of BO_3 overlap with Calcium phosphate band	[31]
A ,B ,C,D	800 –1200	stretching vibrations of the tetrahedral borate units such as (diborate, pentaborate, triborate units	[32]
A ,B ,C,D	1045, 590, 430	Hydroxyapatite	[32]
B ,C,D	1170 –1100	(PO_2) Q_2	[32]
B ,C,D	1200 –1450	B – O stretching of BO_3 units	[33]
B ,C,D	900 – 1200	B – O stretching vibration of tetrahedral $[BO_4]$ units.	[34]
C,D	660	stretching vibrations of P – O –B bonds which form within the meta-phosphate network	[35]
A	around 700	bending of B–O–B linkages in the borate network	[36]
A, B ,C,D	from 450 to 650	bending vibrations of orthophosphate units.	[37]
D	the peak at 930	corresponds to a Ti–O band	[38]
	the peak at 560	Internal modes of PO_4^{-3} ion	[39]
	around 700	due to B-O-B linkages	[40]
	590 and 425	the symmetric stretching of the P–O bonds and O–P–O is bending modes of the Q_0 units	[41]

3.8. SEM of bioactive glasses

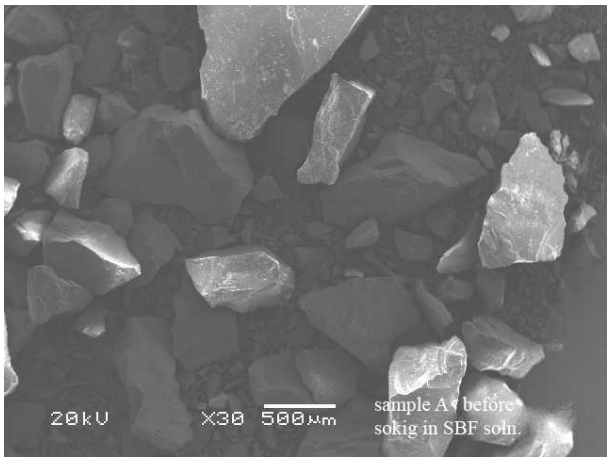
Figure 6 shows the scanning electron microscope (SEM) for different samples. The figure illustrates that hydroxyapatite was present in most of the areas of each studied sample, but some domains of the sample have a dominant presence of hydroxyapatite. This means that the samples were heterogeneous in terms of distribution of hydroxyapatite through the matrix. Larger amount of precipitated particles (representing apatite) is decreasing in glasses with increasing TiO_2 content.



(a) (b)



(c) (d)



(e)

Figure (6): SEM images of glasses soaked in SBF solution for 21 days at 36.5°C for samples (a) glass sample A, (b) glass sample B, (c) glass sample C,(d) glass sample D and (e) SEM micrograph of the glass sample A before soaking in SBF soln.

The SEM micrographs of bioactive glass sample (A) before soaking in SBF solution is shown in Figure 6 - e and the SEM micrographs of bioactive glass samples after soaking in SBF solution for 21 days at 36.5°C are shown in Figure 6 - (a ,b ,c ,d) .

4 DISCUSSIONS

4.1. Density

Density of glasses is increasing with the increasing of the amount of TiO_2 contents into the glass samples. This is obvious because of replacement of P_2O_5 with TiO_2 .the mass of TiO_2 is less than the mass of P_2O_5 ,then the total masses of sample is decreasing with increase TiO_2 concentration and decrease P_2O_5 concentration,. From table 2 the molar volume (V_m) and additive crystalline oxide volume (V_{ox}) are decreasing with increasing TiO_2 concentration and the volume deviation (V_x) is negative, which leads to decrease in volume and increase in the density and causing shrinkage of the glass network[42].

The addition of TiO_2 causes some of the borates structure to change from triangular BO_3 which have a bigger size to tetrahedral BO_4 co-ordination, which have a smaller size of the glass network, which is assured by FTIR diagram. Titanium ions almost exist mainly in the valence state of the form Ti^{4+} in the titled glass network, nevertheless, during the melting and annealing processes of the glasses the reduction of Ti^{4+} to Ti^{3+} can take place.Ti^{3+}ion or [TiO6] enter the glass network and works as a modifier by breaking up B–O–B, B–O–P and P–O–P bonds and forms a non-bridging oxygens (NBO), but Ti ion Prefer react with borate than phosphate network. While the oxygens of these oxides break the local symmetry, Na^+ and Ca^{2+} ions occupy the interstitial positions. This introduces co-ordinate defects which may be called dangling bonds along with non-bridging oxygens (NBO) [43]. IR bands in the figure 5(b) assures the conversion of BO3 to BO4 .The B sample density is high than expected this is due to high concentration of P_2O_5 which act as a decreasing agent in molar volume and the volume of P_2O_5 is larger than the volume of B_2O_3 which lead a net reduction in volume through removal of P_2O_5 [44].

On increasing TiO2 concentration and reducing of P_2O_5 leads to a slow increase in density.

The observed decrease in V_m is affected also by a lower total number of atoms per molecule , when P_2O_5 with seven atoms per unit is replaced by B_2O_3 with five atoms per unit.

4.2. Thermal analysis

The study of B_2O_3 -CaO -Na_2O–TiO_2–P_2O_5 glasses has showed that replacement of P_2O_5 by TiO_2 causes obvious variations in the physico-chemical properties as well as thermal properties of glasses. Thermo-physical properties of glass depend on the structure and composition of the glass.

DTA measurements illustrated that the incorporation of TiO_2 into the structural network of the Boro-phosphate glasses results in a decrease of the glass transition temperature and the crystallization temperature.as shown in figure (1) The temperature difference Tc - Tg can be used as an indicator of thermal stability, whereas the value of this difference is higher the delay in nucleation is more (Mehta et al, 2006). On the other hand, the decrease of the glass transition temperature with increasing titanium oxide content, indicating that Titanium oxide behaves as a structural modifier and depolymerizes the glass network.

The increase in (T_c – T_g) indicate an increase of Chemical durability which is a very important factor to be considered in the commercial application of glasses.

The low value of Tg indicates that the glass sample is thermally unstable and it has a network disruption [45].

Several researchers [46,47] have found that TiO_2 acts as the glass modifier in the form of [TiO6]. A. Yadav [48] reported that TiO_2 would be normally expected to have a coordination number of six for titanium ion in this oxide.

4.3. X-ray Diffraction

Calcium and phosphorus ions are arranged into the layer of the hydroxyapatite, which is formed on the surface of the bulk glass. The above observations lead one to conclude that increasing time of soaking is a dominant factor affecting the formation of a stable apatite layer. Consequently the bioactivity of the redacted material is considered to be a function of the soaking time. Extremely prolonged times, when applied, enhances the bioactivity to its optimum value.

By increasing in TiO_2 concentration in glasses the phosphate concentration is decreased. The calculated Ca/P ratio decreases and tends to be lower than the stoichiometric ratio of pure hydroxyapatite (HA) at 1.67. Such results are in agreement with Lao et al. (2009) [49].

4.4 . Solubility testing

Solubility is an important parameter to recognize the stability of a material which could be used as an implant material in the human body to repair diseased bones or replace damaged bone [50]. Hydrolysis of the borate network in borate glasses take place simultaneously with the leaching of the modifying ions [51]. As the glasses have lower free volumes they dissolve slower [52], and Vitreous B_2O_3 is a highly hygroscopic oxide. As the ratio of TiO_2 increases the percentage of weight loss is found to decrease and addition of different concentrations of TiO_2 to Borate glass helps to increase the durability of the glass. Such result shows that the majorities of the titanium ions in the glasses from B to D are in modifying positions and facilitates for more degradation, whereas in the glasses B, C and D the tetrahedral occupancy of Ti ions prevail and hinders the dissolution. The lower rate of dissolution in the glasses B, C and D can be understood as follows: the substitution ofTi ions prevail over the modifying ions in these glasses as indicated by IR spectra in figure 5 b. In other words TiO_2 is added into the glass network. The titanium ion has a small ionic radius and a large charge, it has the ability to penetrate into the glass network in an interstitial position [53]. Also the decrease of P_2O_5 concentration (from A to D) is due to increase in weight loss and Ph. Similar results have been reported by Aihua Yao et al. [54], and Magyari et al [55] for borate glasses. Therefore, some of the Na^+ and Ca^{2+} ions which are dissolved from glass can be trapped in the porous Ti–rich layer, which would inhibit the reaction between Ca^{2+} and $(PO_4)^{3-}$ to precipitate HA. The process of formation of hydroxyapatite upon the reaction of the bioactive glass sample with SBF involves four stages, which occur very rapidly on the surfaces. These stages are:

1. Fast ion exchange of alkali or alkaline earth with
2. hydrogen ions from SBF solution.
3. Dissolution of glass network by added modifiers, and formation of BO_3 and BO_4 units.
4. Polymerization of borate through consuming Ca^{2+} ions from SBF solution to form electropositive calcium borate layer.

The interaction of the well-formed calcium borate layer with phosphate ions from SBF solution yield calcium phosphate layer (hydroxyapatite).

4.5.pH values

The pH of the residual SBF solution varies after immersion of the glass samples. Such variation is due to the reactions among the glass and the solution at the solid/liquid interface. The variations of pH of the SBF can give a suitable idea about the ambience result from the implanting of glasses into active media. The current results show that the variations of pH occur mainly in the initial immersion period may be up to 180 hours. The increase in pH reveals the dissolution of the glass sample cations in the solution, through exchange with H^+ ions into the simulated body fluid (SBF) solution. The H^+ions are being replaced by cations which cause an increase in OH^- concentration of the solution and pH value. Such conclusion has been confirmed by the curves of the weight loss as presented in figure 3. The variations of pH can be referred to the fact that some ions such as $(BO_3)^{3-}$, Na^+, Ca^{2+} were released from the glass samples into the solution. The variations of pH can be discussed in more details as follows [56]:

(i) Dissolution of Na+ ions.

(ii) Consumption of acidic phosphate ions $(PO_4)^{3-}$ from the glass and the SBF solution to form calcium phosphate layer by reacting with Ca^{2+} ions released from the glass into the solution. To be more specific, Ca^{2+} ions when contaminated with an aqueous solution prefer to be in contact with phosphate anions which are acidic in nature and form calcium phosphate layer on the surface of the glass samples.

(iii) $(BO_3)^{3-}$ ions dissolved from the glass into the solution that may have less effect on pH or it may slightly decrease the pH of SBF [57].

However, it may be worth mentioning here that the corrosion of alkali borate glasses is different from that of silicate glasses. The addition of alkali oxide to B_2O_3 slightly decreases with oxygens and with a nearby alkali borate cation to compensate the excess negative charge. This conclusion is confirmed by FTIR spectra shown in figure 5b.

It is to be noticed that BO_3 phases are more soluble in aqueous media than BO_4 phases [58]. The addition of alkaline earth oxides to alkali borate glass the solubility of glass is expected to decrease due to introducing double charged alkaline earth cations. However, the hydraulic products like the-OH group induce apatite nucleation and the released Ca^{2+} and Na^{+} ions accelerate apatite nucleation in the fluid [59]. The apatite nuclei are formed, they can grow out of the avalanche mechanism by consuming the phosphate and calcium ions from the SBF solution [20].

The increase in pH is considered to contribute to the partial dissolution of the outmost layer and the subsequent apatite precipitation [60] .Also the low in solubility and pH values is due to the less solubility of the glasses when TiO_2 content exceeds 1.0 mol% According to Bunker et al.[61] and Rajendran et al [30].

4.6.FTIR spectroscopy

The bioactivity of glass depends strongly on the exposed surface area to SBF solution. Most of ternary glasses showed bioactivity after soaking in SBF solution within a few days. This has been confirmed by the formation of hydroxypatite phase at their surfaces. The formation of hydroxypatite phase was measured by IR, XRD and SEM.

A second type of bioactive glass was developed here, through the addition of a small amount of TiO_2 (0.02,0.04 and 0.06 mole %) to the glass as an activator agent for apatite formation. The far-IR peaks below 450 cm^{-1} may be attributed to the vibrations of modifier cations in their specific sites.

Bioactivity developed through the addition of activator agents for nucleation such as TiO_2 . This is assured by FTIR data of the glass containing TiO_2 compared with that of glass free from TiO_2. TiO_2 has been reported to have special characteristics that play an important role in enhancing the apatite kinetics in bioactive glass.

Adding TiO_2 to the glass, even with small concentration facilitates the nucleation process [20]. Moreover, the formation of Ti-OH groups beside B-OH ones makes these materials as good candidates for biomaterial developments.

Further, as the concentration of modifying titanium ions is lower, and the concentration of phosphate group decreases then the concentration of NBOs in the glass matrix is lowered. It can be concluded that the degree of localization of the behavior of the glasses depends on the dissolution.

As the titanium oxide increase in the samples , the bioactivity of the material decreased, this behavior Suggests that The formation of HCA layer on the surface of the glass sample causes the termination of the contact between the sample and the SBF solution and this leads to a decrease in pH of the solution [30]. It can be concluded that the degree of localization of electrons decreases (or the donor centers decreases); as a result, the absorption edge shifts towards the shorter wavelength side and the bioactivity is decreasing with titanium oxide concentration rising.

4.7. SEM:

From Figure 6– (a , b, c , d) we note that HA particles have been grown into several agglomerates consisting of needle-shaped HA layer after immersion in SBF solution for more than 15 days at 36.5°C. It was observed that the rate of growth of hydroxyapatite increases on the glass with the decrease of TiO_2 concentration.

5 Conclusion

It is concluded that :

1-The bioactivity of the prepared B_2O_3-P_2O_5-Na_2O-CaO glasses has been controlled through substituting P_2O_5 by TiO_2 progressively.

2- On increasing the TiO_2 concentration which replaces P_2O_5 in the glass, hence P_2O_5 decrease in the glass leading to the decrease of HA layer and hence reducing the glass bioactivity which is assured by XRD and FTIR analysis .

3- The increase in TiO_2 concentration leads to a decrease in solubility of glass when immersed in SBF solution .

References

[1] M.A. Sainz, P. Pena, S. Serena, A. Caballero, Acta Bio mater. 6, 2797-2807 (2010).

[2]D. C. Clupper, L. L. Hench, and J. J. Mecholsky, ''Strength and Toughness of Tape Cast Bioactive Glass 45S5 Following Heat Treatment,'' J. Euro. Ceram.Soc., 24, 2929–43 (2004).

[3] J. Mahamid, Proceedings of the National Academy of Sciences 107 6316 (2010)

[4]Brink M, Turunen T, Happonen R, et al. Compositional dependence of bioactivity of glasses in the system Na2OK2O- MgO-CaO-B2O3-P2O5-SiO2. J Mater Sci Mater Med; 37: 114–121 (1997).

[5] Gerhardt L-C and Boccaccini AR. Bioactive glass and glass-ceramic scaffolds for bone tissue engineering. Materials; 3: 3867–3910 (2010).

[6] Day DE, White JE, Brown RF, et al. Transformation of borate glasses into biologically useful materials. Glass Technol Part A; 44: 75–81 (2003).

[7] Liu X, Xie Z, Zhang C, et al. Bioactive borate glass scaffolds: in vitro and in vivo evaluation for use as a drug delivery system in the treatment of bone infection. J Mater Sci Mater Med; 21: 575–582 (2010).

[8] Jung S. Borate based bioactive glass scaffolds for hard and soft tissue engineering. PhD Dissertation, Missouri University of Science and Technology, (2010).

[9] T. Kokubo, "Bonding mechanism of bioactive glass ceramics A - W to living bone, in: Handbook of Bioactive Ceramics", pp. 41–50 in Bioactive Glasses and Glass Ceramics, Vol. 1, EDS; T. Yamamuro, L.L. Hench, J. Wilson,CRC Press, Boca Raton, (1990).

[10] G. Lusvardi, D. Zaffe, L. Menabue, C. Bertoldi, In vitro and in vivo behavior of zinc doped phosphosilicateglasses ,Acta. Biomaterialia 5, 419 (2009).

[11] D. E. Day, J. E. White, R. F. Brown, and K. D. McMenamin, ''Transformation of Borate Glasses Into Biologically Useful Materials,'' Glass Technol., 44, 75– 81 (2003)

[12] J R Jones. ActaBiomaterialia;9:4457 (2013).

[13] A.H. Yao, D.P. Wang, W.H. Huang, Q. Fu, M.N. Rahaman, D.E. Day, J. Am. Ceram. Soc. 90 303–306 (2007).

[14] A.W. Wren, A. Coughlan, C. M. Smith, S.P. Hudson, F.R. Laffir, M.R. Towler, J. Biomed. Mater. Res Part A 102, 709-720 (2015).

[27] I.M. Asif, R. M. Shelton, P.R. Cooper, O. Addison, R.A. Martin, J. Mater. Sci. Mater. Med. 25, 1865-1873 (2014).

[15] W. Wren, A. Coughlan, K. E. Smale, S. T. Misture, B. P. Mahon, O. M. Clarkin, M. R. Towler, J. Mater. Sci. Materials in Medicine, 23, 2881-2891 (2012).

[16]T. M. Sager, C. Kommineni, and V. Castranova, "Pulmonary response to intratracheal instillation of ultrafine versus fine titanium dioxide: role of particle surface area," Particle and Fibre Toxicology, vol. 5, article 17, (2008).

[17] NIOSH (National Institute for Occupational Safety and Health), "Occupational exposure to titanium dioxide," Publication No. 2011-160, US Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute of Occupational Safety and Health, DHHS (NIOSH), Cincinnati, Ohio, USA, (2011).

[18] T.Morishige, Y. Yoshioka, A. Tanabe et al., "Titanium dioxide induces different levels of IL-1β production dependent on its particle characteristics through caspase-1 activation mediated by reactive oxygen species and cathepsin B," Biochemical and Biophysical Research Communications, vol. 392, no. 2, pp. 160–165, (2010).

[19] C. Ohtsuki, H. Lida, S. Hayakawa, A. Osaka, J. Biomed. Mater.Res. 35, 39-47 (1997).

[20] G. JaganMohini, G. SahayaBaskaran, V. Ravi Kumar, M. Piasecki, N. Veeraiah, Bioactivity studies on TiO2 -bearing Na2O-CaO-SiO2-B2O3 glasses, Materials Science and Engineering C57,240-248 (2015).

[21]A. Saranti, I. Koutselas 1, M.A. Karakassides ,J. Non-Cryst. Solids 352, 390–398(2006).

[22]M.A. Marzouk, H.A. ElBatal, Processing and Application of Ceramics 8 [3] 167–177 (2014).

[23] T.Yano, N.Kunimine, S.Shibata, M.Yamane, J.NonCryst.solids 321, p-157 (2003).

[24] T. Kokubo, T. Kitsugi, T. Yamamuro, J. Biomed. Mater.Res. 24, 721-734 (1990).

[25] M. Vallet-Regí, C.V. Ragel, A.J. Salinas, "Glasses with medical applications", Eur. J. Inorg. Chem., [6], 1029–1042 (2003).

[26] A.M. Abdelghany, H.A. ElBatal, F.M. EzzElDin, "Bone bonding ability behavior of some ternary borate glasses by immersion in sodium phosphate solution", Ceram. Int., 38, 1105–1113 (2012).

[27] M.A. Ouis, A.M. Abdelghany,H.A. ElBatal, "Corrosionmechanisms and bioactivity of bone-glass analogue to Hench's bioglass", Process. Appl. Ceram., 6 [3] 141–149 (2012).

[28] S. Koutsopoulos, J. Biomed. Mater.Res. 62, 600 (2002).

[29] R.K. Singh, A. Srinivasan, App. Sur. Sci. 256, 1725-1730 (2010).

[30]. V. Rajendran, A.V. Gayathri Devi, M. Azooz, F.H. El-Batal, Journal of Non-Crystalline Solids 353, 77–84 (2007).

[31] Mohamed A. Marzouk_, Hatem A. ElBatal Processing and Application of Ceramics 8 [3] 167–177 (2014).

[32] E.I. Kamitsos, "Infrared studies of borate glasses", Phys. Chem. Glasses, 44, 79–87 (2003).

[33] G.D. Chryssikos, M.S. Bitsis, J.A. Kapoutsis, E.I. Kamitsos, J. Non-Cryst. Solids 217, 278 (1997).

[34] AAbdelghany and H Kamal. Ceram Int;40:8003 (2014).

[35] M. Scagliotti, M. Villa, G. Chiodelli, J. Non-Cryst. Solids 93, 350 (1987)

[36] E.I. Kamitsos, A.P. Patsis, M.A. Karakassides, G.D. Chryssikos, J. Non-Cryst. Solids 126, 52 (1992).

[37] K. Nakamoto, Infrared and Raman Spectra of Inorganic and Coordination Compounds, third ed., John Wiley, New York, pp. 143 (1978).

[38] Brow RK. Review: the structure of simple phosphate glasses. J Non-Cryst Solids, 263:1 (2000).

[39] H. B. Pan, X. L. Zhao, X. Zhang, Strontium borate glass: potential biomaterial for bone regeneration, J. R. Soc. Interface 7, 1025–1031(2010).

[40] Ch. Srinivasa Rao, T. Srikumar, Y. Gandi, V. Ravikumar, N. Veeraiah, Philosophical Magazine 91(6) 958-980 (2011).

[41] S. Koutsopoulos, J. Biomed. Mater.Res. 62, 600 (2002).

[42] A. Saini et al. J. Non- Crystalline Solids 355, 2323–2332 (2009).

[43] K.J. Rao, Structural Chemistry of Glasses, Elsevier, Amsterdam, irradiation", Mater. Chem. Phys., 110, 352–362 (2008).

[44] Y.B. Saddeek et al .J. physica B., 403, 2399-2407,(2008).

[45] A. Marikani , A. Maheswaran, M. Premanathan, L. Amalraj. J. Non-Cryst. Solids 354, 3929–3934, (2008).

[46] A. Shaim, M. Et-tabirou, Mater. Chem. Phys. 80, 63–67 (2003).

[47] L. Koudelka, P. Mosner, M. Zeyer, C. Jager, J. Non-Cryst.Solids 326–327, 72–76 (2003).

[48] A. Yadav, C. Gautam , P. Singh NGJC, 2. 126-131. (2012).

[49] Lao J, Nedelec JM, Jallot E, New strontiumbased bioactive glasses: Physicochemical reactivity and delivering capability of biologically active dissolution products. J Mater Chem 19: 2940-2949. (2009)

[50] C.A Lipinski.Adv Drug Del Rev;64:17 (2012).

[51] M. Bohner and J. Lemaitre, "Can bioactivity be tested in vitro withSBF solution?," Biomaterials, 30[12] 2175-79 (2009).

[52]Z. Zhang, K. Hirao, N. Soga, Water corrosion behavior ofdensified glass. II. Borate glasses, J. Non-Cryst. Solids, 135, 62-66 (1991).

[53] J. Am. Ceram. Soc., 86 [8] 1345–52 (2003).

[54] Aihua Yao, Deping Wang, and Wenhai HuangQiang Fu, Mohamed N. Rahaman and Delbert E. Day, J. Am. Ceram. Soc., 90 [1] 303–306(2007)

[55] K. Magyari, R. Stefan, A. Vulpoi, L. Baia, J. of Non-Crystalline Solids 410, 112–117(2015)

[56] Y. Li, M.N. Rahaman, B.S. Bal, D.E. Day, Q. Fu, J. Am. Ceram. Soc. 91, 1528-1533 (2008).

[57] A.M. Abdelghany, Spect. Acta Part A 100, 120-126 (2013).

[58] A.M. Abdelghany, H.A. ElBatal, F.M. EzzElDin, "Bone bonding ability behavior of some ternary borate glasses by immersion in sodium phosphate solution", Ceram. Int., 38, 1105–1113 (2012).

[59] T. Kokubo, H.M. Kim, M. Kawashita, Biomaterials 24, 2161-2175 (2003).

[60] Q Fu. J Biomed Mater Res Part A; 95: 164 (2010).

[61] B.C. Bunker, G.W. Arnold, J.A. Wilder, J. Non-Cryst. Solids 64, 291(1984).