Effect of Transition Metal Addition in the Bioactivity of Borate Bioglass Dental Materials

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Abstract: *Objectives:* The basic structure and some physical properties of a bioactive borate glasses doped with transition metals were prepared and investigated with the same molar composition as 45S5 glass but with all the silicon dioxide (SiO_2) replaced by boron trioxide (B_2O_3).

Methods: The biodegradability was explored and estimated by soaking the samples into simulated body fluid (SBF) at 37ºC for 30 days. The pH changes of solution were measured during the soaking periods in order to explore the ionic change processes. The structural changes in the crystalline phases obtained in the glass matrix before and after immersion in SBF were recognized by means of X-ray diffraction (XRD) and Fourier transform infrared analysis (FTIR). The surface modification was explored by means of scanning electron microscope (SEM).

Results: All obtained results support the aggregation and formation of hydroxyapatite (Hap) layer with different amounts that depend on the type of transition metal added to the glass matrix.

Conclusions: The biodegradation data and spectral analysis of different samples may consider the material to be a good candidate for use as dental biomaterials.

Keywords: Bioactive borate, nanoclusters, biocompatibility, solubility and dental biomaterials.

1. INTRODUCTION

Silicate-based bioactive glasses and glass-ceramics have been widely investigated for bone repair and scaffolds for bone tissue engineering [1]. Most bioactive glasses used as products for sale contain SiO_2 as basic constituent and other types of modifiers. These glasses are demonstrated to be bioactive, a property that can be assessed by analyzing the formation of a nano- hydroxyapatite (Hap) layer on the glass surfaces upon immersion in relevant physiological Fluids [2].

A partial dissolution mechanism is involved in the mechanism of bonding for the silicate based bioactive glasses due to the presence of abundant modifier oxides. The dissolution mechanism results in a formation of a silica gel layer and subsequent precipitation of a calcium phosphate layer [3, 4]. Silicon has a stimulatory effect on proliferation of, contributes to the growth of bone tissue and the bone mineralization process [5].

New studies found that the introduction of reactive borate $(BO_3)^{3-}$ into the glass network provides an approach to achieving the requirements of both degradations and bioactivity for tissue engineering [6]. Bioactive borates show a fast degradation behavior and form a more rapid hydroxyapatite conversion rate in the simulated body fluid than bioactive silicates. Also, the degradation rate of bioactive borates can be controlled by adjusting the content of in the glass [7]. Porous scaffolds of a bioactive borate glass with the composition obtained by replacing all the SiO_2 glass with B_2O_3 has shown the capacity to support soft tissue infiltration when implanted in rat subcutaneous sites [8]. Boron-modified 45S5 glass supported faster new bone growth than 45S5 glass [9]. Many bivalent trace metallic ions have showed beneficial effects in bone tissue engineering applications. Realistic rebuttal in different studies shows that Zn^{2+}, Cu^{2+}, and Co^{2+} ions play a vital role in osteogenesis and angiogenesis or in both cases. Bioactive materials containing these additives are able to bond directly with the bone and can be considered as bone-repairing materials in clinical applications [10]. It is well known that there are two main mechanisms for apatite formation on the surface of materials based on soaking in SBF. The first one is the release of some ions from the surface and bulk of material to form a negative charge on the surface attracts phosphorus from solution and form apatite. The second mechanism provides a nucleation site in a specific microstructure on microscale [11].

In this paper, new types of bioactive glass contain different types of transition metals were prepared and

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investigated from the viewpoint of their activities. These species of transition metal doped bioactive borate glasses have not been studied previously. These glasses possess compatibility behavior and a controllable degree of degradation which make them suitable to be used in field of tissue engineering and dental materials preparation.

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In this paper, new types of bioactive glass contain different types of transition metals were prepared and investigated from the viewpoint of their activities. These species of transition metal doped bioactive borate glasses have not been studied previously. These glasses possess a controllable degree of degradation and compatibility which make them suitable to be used in the field of tissue engineering and scaffold manufacturing.

2. EXPERIMENTAL PROCEDURES

2.1. Preparation of Bioactive Glasses

Glass samples were prepared by replacement of B_2O_3 (glass former) replacing SiO_2 (glass former) in the patented Hench's bioglass using chemically pure H_3BO_3, $CaCO_3$, Na_2CO_3, and $NH_4H_2PO_4$. Using nominal composition (48.63 B_2O_3, 22.92 Na_2O, 22.86 CaO, and 5.59 P_2O_5) wt%, some bioglasses were prepared with addition of 3d transition metals were introduced (2 wt %) in the form of their following oxides: TiO_2, V_2O_5, Cr_2O_3, MnO_2, Fe_2O_3, CoO, NiO and CuO. The batches were accurately weighed out and then melted in porcelain crucibles using an electric furnace at 1150 ^oC for 2 h and the melts were shacked well several times to achieve homogeneity. Each melt was stirred by rotating the crucible several times every 30 mins. The homogeneous melts were cast after 2h of melting into preheated stainless steel molds.

2.2. Preparation of Simulated Body Fluid (SBF)

Simulated body fluid was prepared by the chemical which give ionic concentrations which are nearly identical to that of human plasma.

Table 1: Chemical Composition for the Prepared the Simulated Body Fluid (SBF)

Reagent	NaCl	$NaHCO_3$	KCl	$Na_2HPO_4.2H_2O$	$MgCl_2.6H_2O$	$CaCl_2.2H_2O$	Na_2SO_4	$(CH_2OH)_3CNH_2$
Amount (g/l)	6.457	2.262	0.373	0.178	0.305	0.368	0.071	6.057

2.3. X-ray Diffraction Analysis

The identity of the crystalline phases formed within the samples before and after immersion was analyzed by X-ray diffraction technique in order to identify the structural changes. The samples were ground and the fine powder was examined using a diffractometer adopting Ni-filter and Cu-target. The X-ray diffraction patterns were obtained using a Philips PW1390 X-ray diffractometer. The crystallinity indices were measured by materials studio software version 5.5.1.

2.4. Solubility Testing

The solubility of glasses was evaluated by the measurement of mass loss in simulated body fluid (SBF) at 37 °C in the incubator. Samples were polished with a 600 grit polishing paper, washed by acetone ultrasonically for a few minutes, and then placed in polyethylene beaker containing pre-calculated volume of SBF solution so the ratio between geometric area of the glass samples and volume of the solution was fixed as 0.075 cm^{-1} in all cases for comparison and to avoid defects resulting from volumetric differences. Samples were removed and excess moisture was removed by tissue paper at various time intervals and then reweighed. The percent changes of mass loss were correlated to glass solubility or corrosion. Solubility measurements were carried out in triplicate for obtaining acceptable mass loss measurements.

By knowing the initial weight (M_0) of each sample and the mass loss (M_t) at time t, the % of mass loss per unit area was obtained as:

$$Mass \quad loss\,(\%) = \frac{M_0 - M_t}{A} x100 \qquad (1)$$

Where a is the surface area in cm^2.

2.5. pH Measurements

Changes in solution pH are very important to analyze when bioactive glasses are dissolved in simulated body fluids. pH values are easily measured with a pH-meter (Jenway-3150 Premier Portable pH/mV/ Temperature Meter with an accuracy of 0.01). The calibration of the electrode against buffer solution was performed at an interval of 24 h.

2.6. FTIR Measurements

Fourier transform infrared absorption signals of the studied borate glasses were measured at room temperature (20°C) in the wavelength range 4000-400 cm^{-1} using a computerized recording FTIR spectrometer (Mattson5000, USA). Fine powdered samples were mixed with KBr in the ratio 1:100 for quantitative analysis and the weighted mixtures were subjected to a load of 5t/cm^2 in a revocable i.e to produce clear homogenous discs. Then, the IR absorption spectra were immediately measured after preparing the discs to avoid moisture attack. The FTIR measurements were repeated after the samples were immersed in SBF.

2.7. Surface Structural Analysis Using Scanning Electron Microscopy

Scanning electron microscopic (SEM) investigations were performed on glass samples at room temperature using an SEM model Philips XL30 attached with EDX unit, with accelerating voltage 30kV, magnification up to 400,000. All surfaces of studied samples were coated with gold for morphological investigations.

3. RESULTS AND DISCUSSION

3.1. pH Measurements

It is well known that mechanisms by which silicate, borate, and borosilicate bioactive glass degrade and convert to an Hap-like material have been the main subject of several investigations [9]. The degradation kinetics of the glass and conversion mechanism to Hap *in vitro* have been evaluated by immersing the glass (in the shape of particles, a disc or a porous scaffold) in an aqueous phosphate solution such as SBF at 37 °C then measuring the mass loss of the glass as a within time of immersion [6].

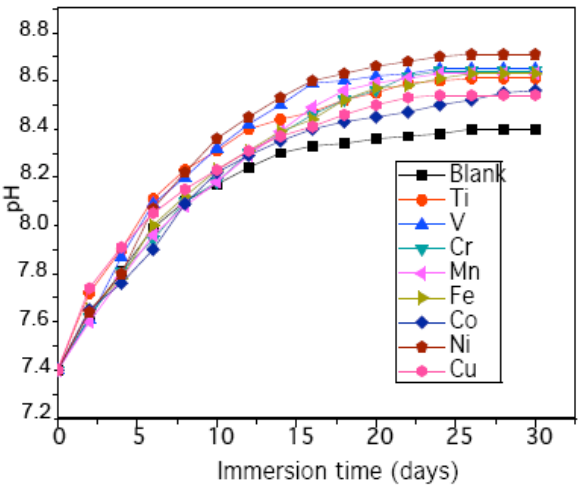


Figure 1: Changes in pH values of the SBF at different time intervals.

Figure **1** illustrates the changes that occur in the pH upon addition of glass samples within simulated body

fluid. The change in pH was recorded at different time intervals up to 30 days of immersion. The pH value of SBF starts from pH value ≈ 7.4 and approaches a nearly constant value that depends on the type of transition metal added to the glass matrix. The ph increase occurs when all samples are soaked into solution, regardless of the type of transitional element added. The degradation is accompanied by the dissolution of ions and soluble species (e.g. Na^+ and $(BO_3)^{3-}$, depending on the composition of the prepared glass) into the solution and leaching of cations out of the glass, which are further exchanged sodium ions with that of H^+ ions from the solution, so there is also a change in the pH and the ionic concentration of the solution as a function of time. In addition, the conversion product has been characterized using structural, chemical and micro-chemical techniques [13].

The lowest change in pH value, both in rate and magnitude, was observed for base bioglass composition since the pH immediately raised from ~7.4 to ~8.1 during the first 15 days of immersion. Then, it increased slightly nearly another pH ~8.3 in the following 15 days. In sample with 3d transition metal nickel (Ni containing glass), a rapid increase from 7.4 to ~8.6 in the first 15 days followed by an increase from ~8 to ~8.7 in the other following days of immersion.

The concentration and type of transition metal species strongly influence the acid/base properties of the bioactive glass surface. Also, the amount of Ca plays an important role in the interaction of glass and SBF [14]. Molar adsorption heats developed by the interaction of bioactive glasses and SBF indicate the possibility of cooperative effects among calcium cations when the latter are present in relatively high amounts [15].

3.2. Mass Loss and Solubility

The addition of sodium to borate glasses was reported to increases the chemical durability since it decreases the mass loss. Also, the addition of P_2O_5 into glass serves to decrease the durability of glasses [7]. Figure **2** shows the percent mass loss of all prepared glass samples during different immersion periods. The prepared glasses possess a considerable degree of degradability greater than that in case of silicates; this is because the prepared samples experience a mass loss approximately 3.5% in about 15 days of immersion in SBF. All results in mass loss measurements agree well with that obtained for other well-accepted soluble bioactive glassy compositions.

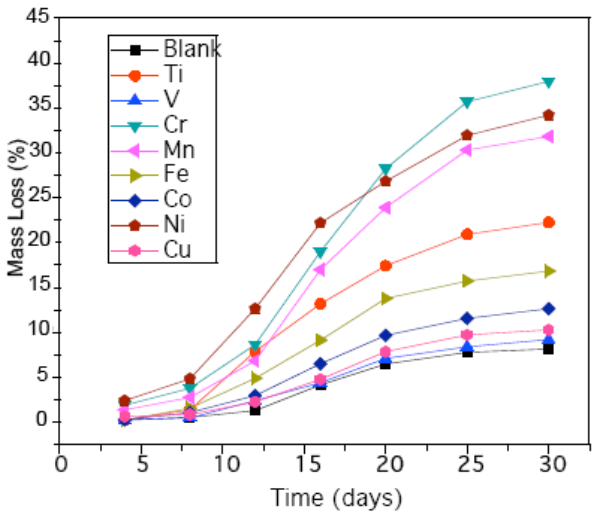


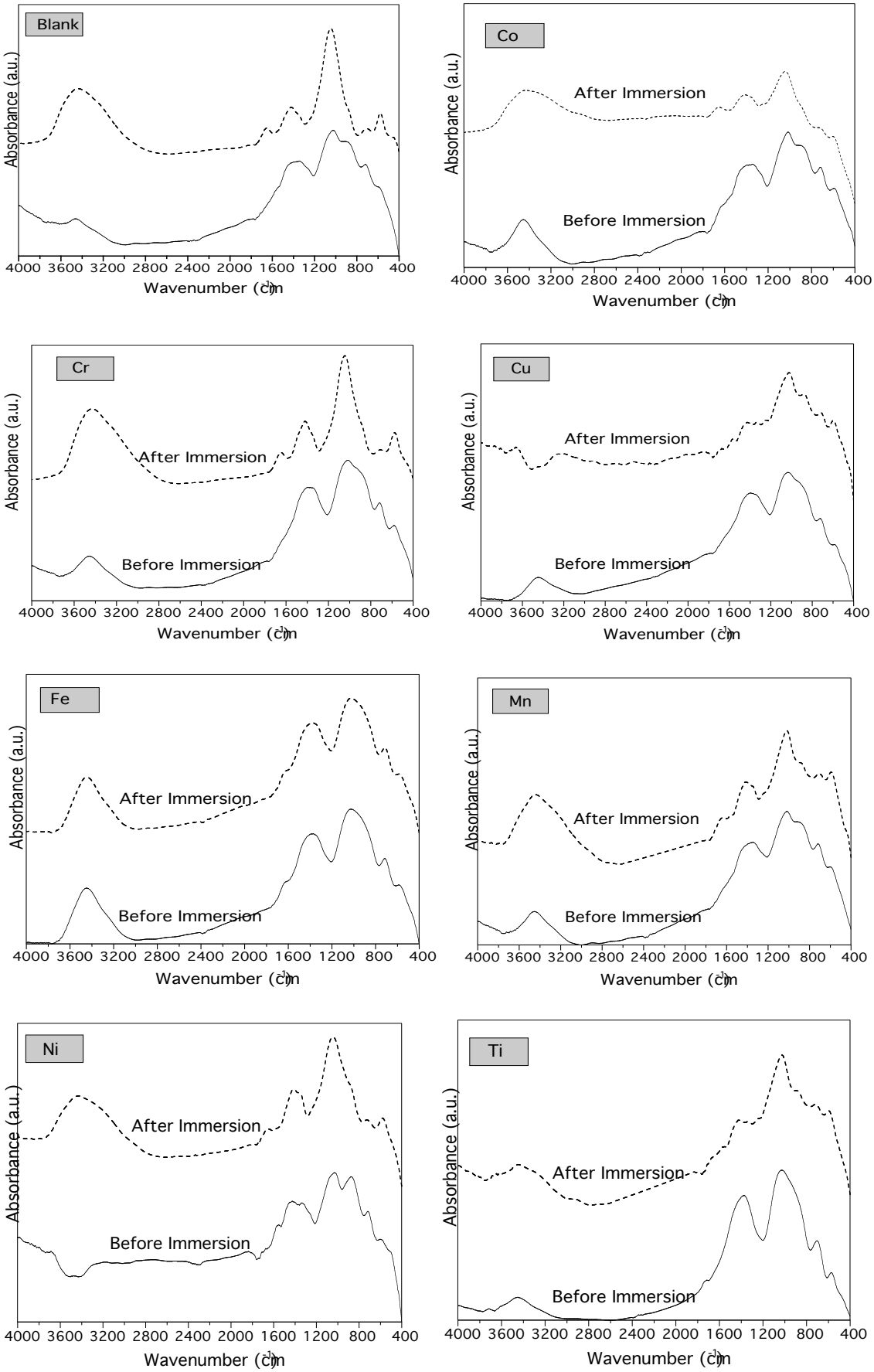
Figure 2: Mass loss for glass samples soaked in SBF solution at 37 °C as a function of time.

3.3. Interpretation of the FTIR Spectra of the Studied Borate Glasses before Immersion in SBF

Infrared (IR) spectroscopy is one of the most important spectroscopic techniques used by organic and inorganic chemists. The main goal of IR spectroscopic analysis is to determine the chemical functional groups present in the sample. X-ray diffraction analysis (XRD) fails to identify the local structural building units within glasses and even to differentiate between various glass systems due to the lack of long-range order. So, IR spectroscopy is considered to be a popular tool for structural elucidation and compound identification.

However, infrared spectroscopic analysis has been approved to be used to confirm the corrosion mechanism in some glasses and to verify various structural building units in glasses and even low concentration impurities such as modifier cations, water, and hydroxyl groups, also to confirm bone bonding ability or bioactivity in silicate and borate bioglasses.

Figure **3** Illustrates the FTIR spectra of the prepared borate glasses before and after immersion in SBF. The structure of vitreous B_2O_3 consists of triangular borate (BO_3) units arranged mostly in boroxol groups [6]. Addition of alkali oxide (e.g.Na_2O) or alkaline earth oxide (e.g. CaO) changes some of the triangular borate units into tetrahedral (BO_4) units. After a certain limit of addition the formation of more BO_4 groups ceases and the surplus modifier oxide forms non-bridging oxygens. The prepared bioactive borate glasses are expected to contain both tetrahedral (BO_4) and triangular (BO_3) units with ratio depends on the composition of glass constituents [1].


Blank
Co
Cr
Cu
Fe
Mn
Ni
Ti
After Immersion
Before Immersion
Absorbance (a.u.)
Wavenumber (cm-1)
4000 3600 3200 2800 2400 2000 1600 1200 800 400

(Figure 3 Continued)

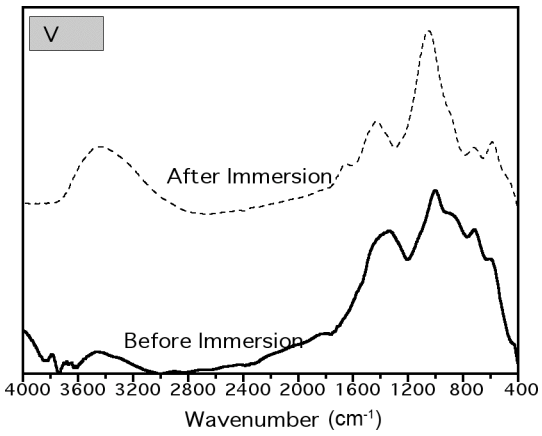


Figure 3: FTIR spectra of the prepared glasses before and after immersion in SBF for 30 days.

The observed FTIR spectra of the studied glasses can be realized and interpreted as follows [15]:

- The band in the range of 650–800 cm^{-1} is due to bending vibrations of B–O–B groups in [BO_3] triangles.
- Absorption band between 900 and 1200 cm^{-1} was observed due to B–O stretching vibration of tetrahedral [BO_4] units.
- The FTIR characteristic peaks of phosphate groups appear in the form of a strongest band at 1035 cm^{-1} attributed to P–O stretching vibration.
- The far-IR peaks below 450 cm^{-1} can be related to vibrations of modifier cations in their specific sites.
- The absorption bands at wavenumber range of 1250–1600 cm^{-1} are attributed to the bending vibration and stretching vibration of B–O–B in BO_3 triangles.
- The small curvature at 1400 cm^{-1} is due to carbonate group.
- The small peak at about 1630 cm^{-1} is related to molecular water.
- The two small peaks at 2852 and 2922 cm^{-1} are related to water, OH vibrations.
- The broad near IR band centered at 3434 cm^{-1} is due to molecular water.

3.4. Interpretation of the IR Spectra of the Studied Borate Glasses after Immersion in SBF

Figure **3** illustrates that the FTIR spectra for the studied borate glasses after immersion in SBF solution for 30 days.

The graph represents some of the observed changes:

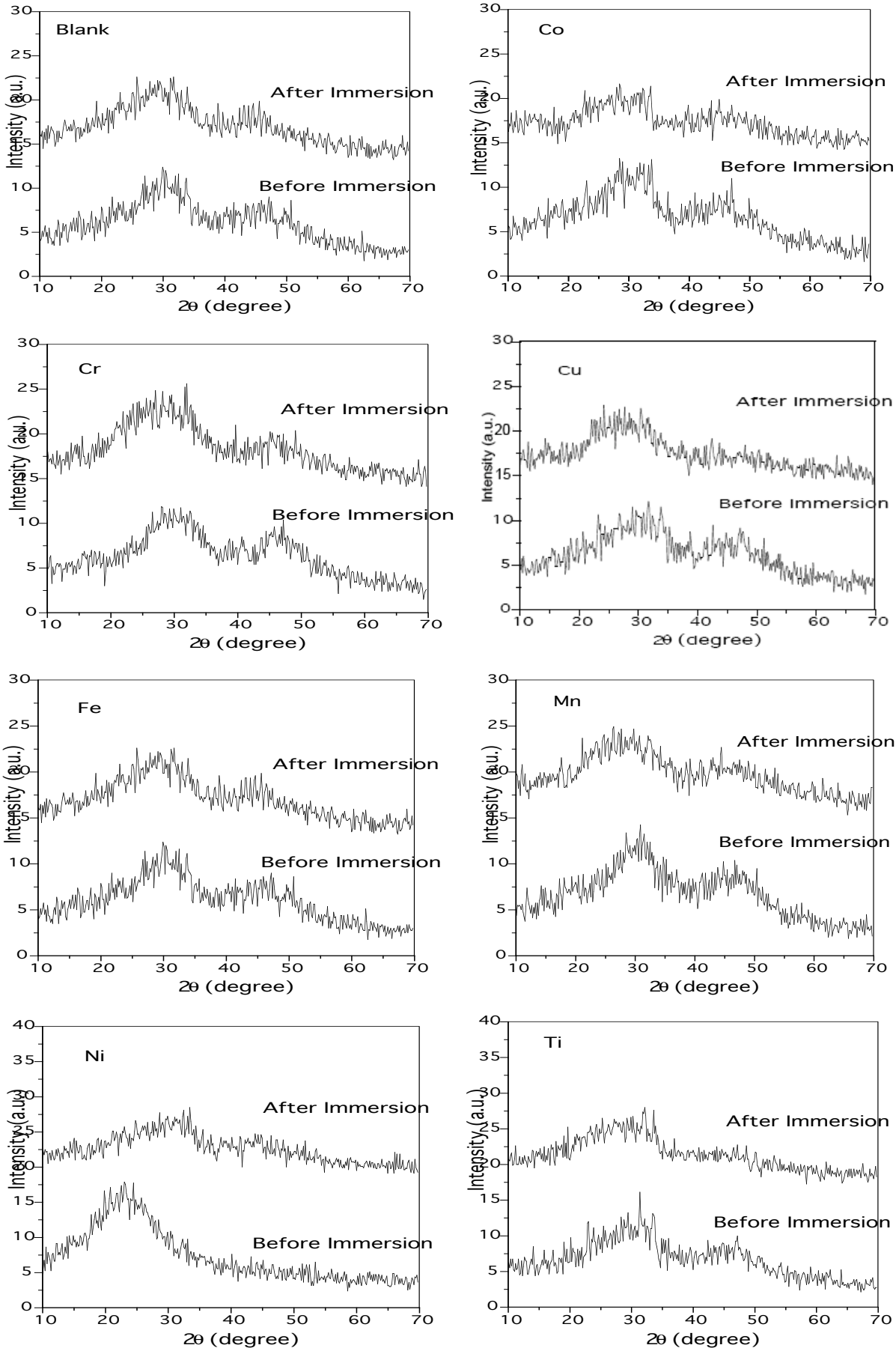
The strong resolution and presence of the band at 1050 cm^{-1} is accompanied with the observed decrease of the intensity of the bands in the range of 1200–1500 cm^{-1} which may indicates the decrease of the BO_3 groups and the persistence of the BO_4 groups. This behavior is evident that it is well related to dissolution of the BO_3 bearing phases which are very weak in comparison with the strong BO_4 groups in which each boron atom is attached from the four directions by alkali or alkaline earth cation to cause neutrality [13].

The IR absorption bands recorded from the samples surface after 30 days immersion in SBF are consistent with the spectra for apatite compositions. P–O bending vibration arises from and that recorded in the spectral range 620–560 cm^{-1}. This specific split is attributed to the presence or precipitation of calcium phosphate or hydroxyapatite. This band is a good indication of a potential bioactivity of the studied borate glasses. The peak at 1640 cm^{-1} is correlated with hydroxyl groups $(OH)^-$ [6]. Bands of phosphate groups are similar to that of the blank and are assigned to P–O bending and stretching vibrations. The width of the absorption band is related to the crystallinity of self-assembled surface layer and this reflects disorder degree of the hydroxyapatite type layer that formed on the surface of samples.

3.5. X-ray Diffraction

Figure **4** shows the X-ray diffraction (XRD) patterns of the prepared glass samples before and after immersion in the SBF for 30 days.

It can be noted from this Figure that the pattern of this type of these glasses exhibits weak diffraction lines


Blank
After Immersion
Before Immersion
Co
After Immersion
Before Immersion
Cr
After Immersion
Before Immersion
Cu
After Immersion
Before Immersion
Fe
After Immersion
Before Immersion
Mn
After Immersion
Before Immersion
Ni
After Immersion
Before Immersion
Ti
After Immersion
Before Immersion
Intensity (a.u.)
2θ (degree)

(Figure 4 continued)

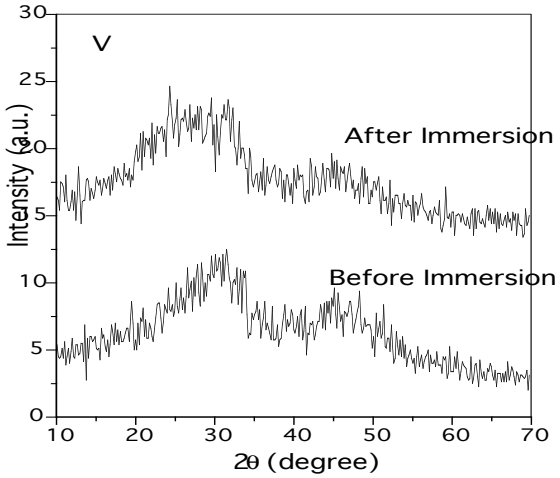


Figure 4: X-ray diffraction pattern of glasses before and after30 days of immersion.

superimposed on two broad humps one of them extend from 2θ range from 15° to 35° and the other one extent from 40° to 60°. Broadening of the peak is clearly evident and indicates the amorphous nature and/or poor ordering of this glass. All glass samples appears to contain some minor crystalline phases in nanoscale which are sodium phosphate oxide $Na_5P_3O_{10}$ (JCPDS 02-0923), calcium phosphate $Ca_3(PO_4)_2$ (JCPDS 70-0364), and calcium borate CaB_2O_4 (JCPDS 22-0141), and with different ratios in addition to other minor phases depending on the glass composition [14].

The hump extends from 2θ range 40° to 60° was found to be decreased within immersion time of 30 days and this may be related to change in crystallinity. The degree of crystallinity was measured to all glass samples before and after immersion, it was found to increase for all samples with a percent range between the values (1.7 % to 9.88 %). In Figure **5**, the degree of crystallinity (%) was plotted against the type of transition metal type before and after soaking in SBF. It is well known the concentration of TiO_2 play an important role in volume crystallization. In our prepared glass, the addition of (2 wt%) decreases crystallization in borate matrix. So, examination of the previous crystalline phases that are formed during immersion of glassy samples in SBF indicates that the concentration of and type of transition metal added play an important role in crystallization of all the prepared glasses.

In silicate bioglass (45S5), this type can be easily crystallized and forms the main phase of sodium calcium silicate solid solution [15]. This is may be due to the presence of both phosphate and silicate networks together and the possibility of obvious phase separation upon preparation. It is well known by various scientists that the addition of few percent of P_2O_5 plays an important role to promote volume nucleation and crystallization [16]. There is some evidence that precipitated phosphate crystals subsequently act as heterogeneous nucleation sites for the formation of major phases.

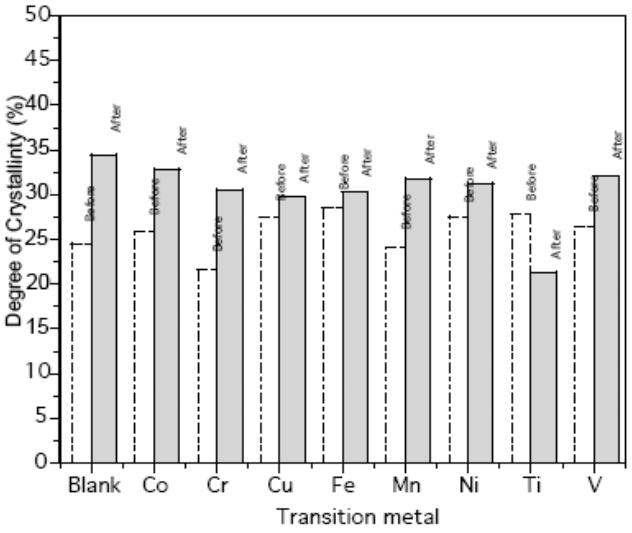
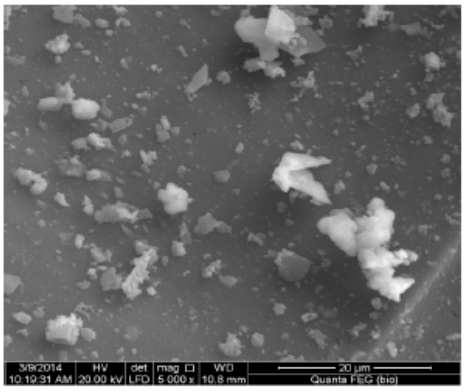
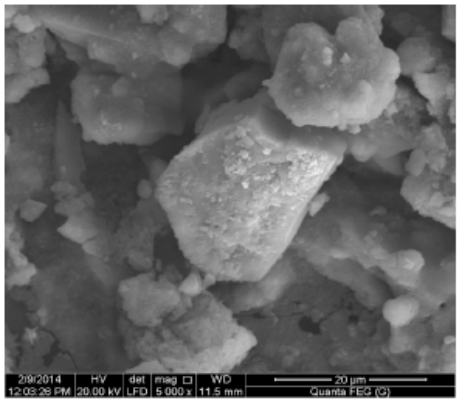


Figure 5: Degree of crystallinity of prepared glasses before and after 30 days of immersion.

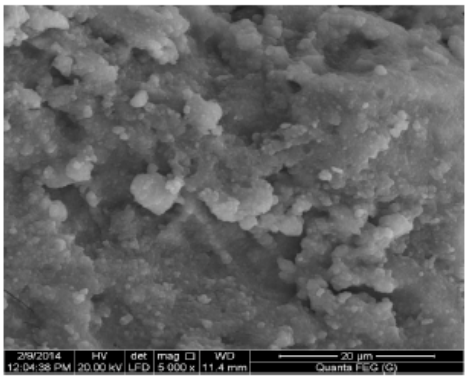
The obtained hydroxyapatite Ca_{10} $(PO_4)_6$ OH_2 (JCPDS 72-1243) phase is poorly crystallized and is considered to be in the amorphous form or it may be in a nanoscale size [6]. The small concentrations of hydroxyapatite in the sample were not easily be detected because this technique is not sensitive to minor concentrations of hydroxyapatites. FTIR technique is considered to be a more sensitive technique if we compare it with XRD technique for monitoring the formation of hydroxyapatite on the surfaces of the glass particles FTIR results support the precipitation of HA in our prepared glasses since the bending and stretching vibrations of P-O is arises in the spectral range 620-560 cm^{-1} and is attributed to the presence or



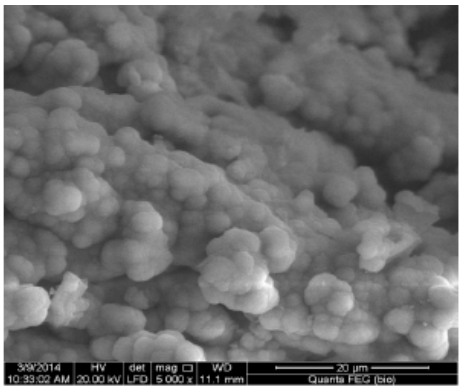
(**A**) Blank



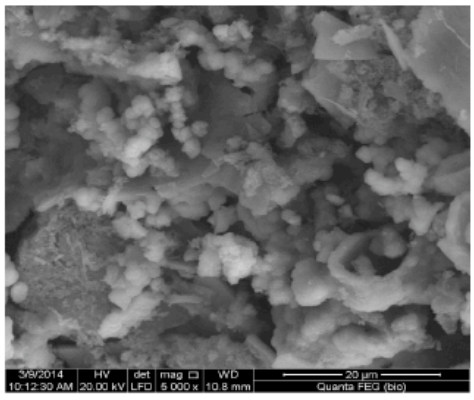
(**B**)Co



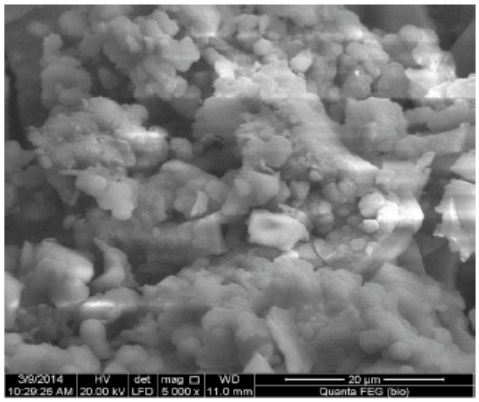
(**C**) Cr



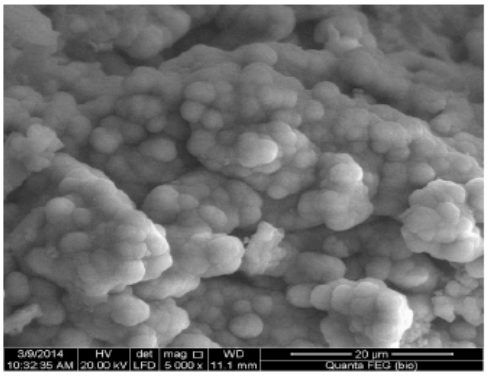
(**D**) Cu



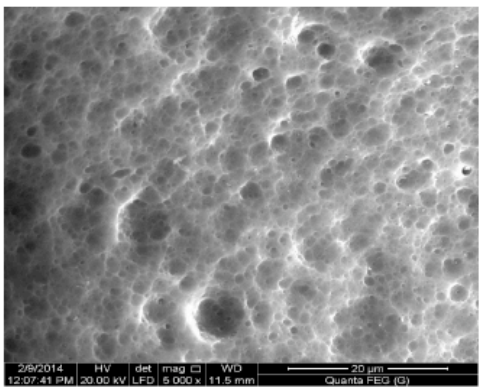
(**E**)Fe



(**F**)Mn

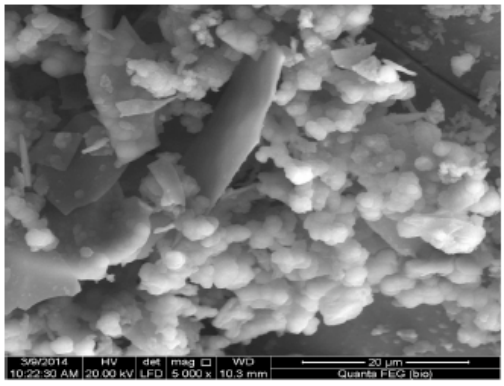


(**G**) Ni



(**H**) Ti

(Figure 6 Continued)



(I)V

Figure 5: Scanning electron micrographs of glasses after 30 days of immersion.

precipitation of calcium phosphate or hydroxyapatite. It is well known that calcium and phosphorus ions are arranged into the hydroxyapatite layer which is formed on the bulk glass surface.

3.6. Surface Structural Analysis Using Scanning Electron Microscopy

One of the main goals of nanocluster science is the ability to prepare nanoclusters with a very narrow size distributions allowing for greater uniformity of nanocluster properties [17]. The nucleation and growth of metal nanoclusters solution has been the subject of increasing study at the nanometer scale [18]. This nucleation process is very sensitive to the size and shape of transition metal added. So, the electronic, optical, and catalytic properties of nanocluster are affected by it.

Our considerations based upon SEM observations agree well with those previously reported results. Both indicate that, when bioglasses are soaked in SBF for long reaction time (30 days), the hydroxyapatite layer can be formed and precipitated on the surfaces rich with functional groups (M-OH) where M is the type of transition metal added. For example in cases of Ti, the formed functional groups are Ti-OH. Some authors have reached the conclusion that the presence of some groups is known as the promising candidates for supplying inducers for the apatite formation With further increase in soaking time, the hydroxyapatite spreads over the entire surface and a highly concentrated layer of hydroxyapatite could be observed as shown in Figures (**5A** to **I**). Our SEM data can be explained by assuming that transition metal ions in the doping level (2wt %) seem to act as nucleating agents promoting nucleation and crystal growth of hydroxyapatite. Numerous scientists have assumed that transition metal oxides are efficient nucleates in the volume crystallization of glasses. It seems that further detailed studies are needed to justify the role of each transition metal from the 3d-elements by combined techniques in promoting bioactivity of the prepared glasses.

CONCLUSIONS

FTIR spectra of glasses confirm clearly the precipitation of hydroxyapatite on the glass surface upon immersion in solution. SEM technique was used to examine the morphological changes of the surfaces upon immersion and the effects of different individual transition metals additives. pH change supports the ion exchange occurs between the glass and solution. The role of transition metal is extensively discussed and their role as nucleating agents to promote nucleation and crystal growth of hydroxyapatite is explored. From all obtained data, the studied glasses are capable of reaction with SBF and the additives of transition metal did not obstruct the process of dissolution and precipitation of hydroxyapatites. The suitability of the prepared glasses to be used as bone scaffolds and tissue engineering science comes from the spectral and solubility measurements.

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