Immobilization of boronic acid derivative onto the magnetic Gd-containing composites

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Abstract. Aiming to develop new magnetic materials for neutron shielding applications, B- and Gd-containing magnetic nanoparticles were synthesized. Following bottom-up synthetic approach, core-shell $\text{Fe}_3\text{O}_4/\text{Gd}_2\text{O}_3$ nanocomposite particles were synthesized at the first stage. In the next stage, magnetic core-shell particles were modified with amino groups followed by grafting onto their surface of the boronic acid derivative. Such a multifunctional material, containing both boron (B) and gadolinium (Gd) atoms is a promising candidate for developing films and membranes, strongly interacting with neutrons. Due to the presence of boronic acids and bound to the indicator (Alizarin Red S), the material can induce color changes while immersed in sugar-containing solutions. Such a feature enables a possibility to estimate the number of boron atoms left after interaction with neutrons, thus allowing to check composite neutron-capture recourse.

1. Introduction

Research aimed at creating supramolecular, composite, nanostructured, and consolidated materials that effectively absorb ultrahigh-frequency electromagnetic and neutron radiation for use in technical, medical-biological, environmental, etc., has become significant in our time. Nanocomposites that are sensitive to effectively adsorb neutron radiation are promising for practical implementation in radiation medicine, engineering, ecology, biology, and more. However, there is still a need for development, not just efficient materials, but materials from sustainable sources.

In this view, gadolinium, and boron, chemical elements with high neutron capture cross-sections, are attractive due to their versatile chemistry and ability to be incorporated into re-processible composites. In the case of boron, it interacts with epithermal neutrons with the release of gamma-quants and alpha-particles, as shown in the scheme below (figure 1).

Alpha-particle have free path lengths in the range of micrometers, and thus, to avoid secondary radiation damage to the material caused by alpha-particles, boron components can be incorporated into a layered matrix, preferably of inorganic oxide origin. Such an inorganic matrix can be an iron oxide, due to its good radiation-scavenging properties. Also, if such an
oxide contains gadolinium components, it can work as a secondary barrier for the neutrons. For instance, the enhancement of neutron attenuation and reduction in secondary gamma by combining $Gd_2O_3$ and $B_4C$ has been shown in work [1].

In literature, a gadolinium oxide $Gd_2O_3$ was used for the preparation of self-healing poly (vinyl alcohol) hydrogels for thermal neutron shielding [2]. Also, a $Gd_2O_3$ based thermal neutron attenuating paint with an oxide mass fraction of 0.4 has been produced using commercial polyurethane and has shown good neutron protection properties [3]. In another example, nano-boron carbide ($B_4C$) and boron nitride (BN) particle-reinforced polymer composites were developed for neutron shielding [4]. However, to increase the interfacial adhesion between BN and the polymer matrix, additional modification with coupling agents is needed [5], which might cause additional expenses. For this purpose, a $B_4C$/epoxy composite was developed [6]. However, the thickness of such a coating for 80% absorption of neutron fluence was almost 9.8 mm at 3 wt% of $B_4C$ (particles 150µm). This result proves that high loading of neutron-shielding materials is needed. To another publication [7], a nanoamorphous $B_2O_3$ layer was designed and fabricated between $B_4C$ particles and an Al matrix. The authors claim that good corrosion resistance makes $B_4C@B_2O_3/Al$ composites a potential neutron shielding material. Also, the addition of medium-heavy metal powders to epoxy-based composite was proposed as an effective way to improve the neutron-shielding properties of materials [8].

Thus, a hierarchical structure, containing layers of boron components alternating with mixed gadolinium/iron oxide seems to be most attractive in terms of scavenging neutron radiation, and such a material was developed in this work.

2. Experimental part

**Synthesis of magnetic Gd-containing nanosized carrier.** Doping of magnetite’s surface with gadolinium ions was carried out with gadolinium nitrate. Briefly, the solution containing ferrous and ferric salts (1M: 2M), and 1 mole of $Gd(NO_3)_3$, was heated to 90 °C, and slowly precipitated by the addition of ammonia solution under vigorous stirring. Precipitated $Fe_3O_4/Gd_2O_3$ nanocomposite particles were washed with distilled water until a neutral pH and separated with a permanent magnet and sonicated twice for 5 minutes. The average particle size was ~13 nm. The particles were stabilized either with sodium oleate or oleic acid.

**Modification of the surface of magnetic Gd-containing by γ-aminopropylsiloxane.** The surface of magnetic Gd-containing nanoparticles was coated with γ-aminopropylsiloxane (γ-APS) in toluene [9]. The reaction of polycondensation is carried out according to the scheme in (figure 2).

Transmission electron microscopy (TEM) of magnetite nanoparticles was performed using transmission electron Microscope JEOL 2010.

γ-APS was dried over molecular sieves and purified by distillation in a vacuum. Magnetic Gd-containing particles were exposed to a solution of γ-APS (10% vol.) in toluene for 8 h, precipitated in a centrifuge, washed with toluene and acetone, and dried at 293 K. Contents

![Figure 1. Interaction of boron with epithermal neutrons.](image-url)
of functional groups on the surface of magnetite were measured with X-ray photoelectron spectroscopy (XPS) and differential scanning calorimetry (DSC) combined with differential thermogravimetric analysis (DTA). The thermal graphs were recorded in the temperature range 293–1273 K at the heating rate of 0.16 °C/s on a Q-1500D thermal analyzer purchased from the company MOM (Hungary) [10,11].

**Immobilization of boronic acid derivative.** 5-formil-2-furyl boronic acid (furyl borate) was immobilized on the surface of Magnetite/3-APS composite in ethanolic solution. Immobilization of Alizarine Red S was performed in phosphate buffer (pH=7.4).

3. Results and discussion

To create neutron-shielding materials which are safer for the environment, we have selected a boronic acid derivative. This is due to their relatively low toxicity and their degradation into the environmentally benign boric acid [12].

From the DTA data was calculated, the concentration of the hydroxyl groups on the magnetic Gd-containing nanoparticles (specific surface area Ssp= 90 m²/g) was equal to 2.4 mol/m² or 2.2 mmol/g [9]. On the surface of magnetite forms Si-O-Si use polymeric coating a with high degree of polymerization which, in its turn, can further provide magnetic carriers with certain chemical or biochemical properties.

The nano-dimentsiality of synthesized magnetite particles was confirmed by electron microscopy (figure 3a). The presence of the amino groups at the surface of the obtained nanocomposite was confirmed with XPS [9]. The obtained samples were tested by Fourier-transform IR-spectroscopy. Figure 3b shows the Fourier-IR spectrum of magnetite, modified by γ-APS. Pronounced absorption bands at 1037 and 1130 cm⁻¹ of approximately equal intensities indicate the formation of a polymer layer of Si–O–Si at the magnetite surface resulting from hydrolytic polycondensation of the modifier molecules. Intensive doublet at 1037 and 1130 cm⁻¹ is caused by the formation of polymer structure with a high degree of polymerization, i.e., on the surface of magnetite occurs hydrolytic polycondensation of molecules of modifier with the formation of polymer structure of the bonded layer of a modifier [9,10].

Thus, having modification of magnetic Gd-containing nanosized carrier confirmed, we have proceeded with immobilization of the boronic acid derivative (figure 4). Synthesis of Fe₃O₄/3-APS/furfurylborate nanocomposite showed below.

FTIR-spectra (figure 5) shows AB at 1732 and 1811 cm⁻¹, that corresponds to a formyl residue of initial furfurylborate. Splitting to two AB can be explained by a possible intermolecular interaction of formyl residue with hydroxyl groups of boronic acid. After furfurylborate interaction with amino group of modified magnetite, AB of formyl residue disappears, that confirm formation of Fe₃O₄/3-APS/furfurylborate nanocomposite. AB of -B=C bond can be observed at 900 cm⁻¹, AB of -B= bond appear at 1350 cm⁻¹. Adsorption bands of -C=N bond can be observed at 1630-1690 cm⁻¹. Thus, IR spectroscopy confirms that furfurylborate has been successfully immobilized on the surface of Gd-containing magnetic particles.

Boronic acids contain trivalent boron atoms bonded to one alkyl/aryl substituent and two hydroxyl groups \(R-B(OH)₂\) [13]. Unique and versatile reactivity [14] and stability [12] of boronic acids have led to uses in numerous areas, including C-C bond formation, acid

\[ \text{[–OH + \{(C₂H₅O)₃Si(CH₂)₃NH₂] → [–O–Si(CH₂)₃NH₂ + 3C₂H₅OH} \]

**Figure 2.** Polycondensation reaction scheme.
Figure 3. TEM image of initial magnetite particles (a), and FTIR spectra of magnetic Gd-containing nanosized carrier modified by γ-aminopropylsiloxane (b).

Figure 4. Scheme of immobilization of boronic acid derivative.

catalysis, asymmetric synthesis, carbohydrate analysis, metalcatalysis, molecular sensing, and as therapeutic agents, enzyme inhibitors, and novel materials [13]. Perhaps the most important chemical characteristic that has led to boronic acids finding utility in a plethora of biomedical applications is the ability to form reversible covalent complexes with 1,2- or 1,3-diols [12] (figure 6).

For instance, ARS dye (figure 7), an a cis-diol has been used as a reagent for the fluorometric determination of boric acid interactions with cis-diols [15].

ARS displays a dramatic change in fluorescence intensity and color in response to the binding of boronic acid [16]. Thus, there is a “switch” of ARS molecules from a non-fluorescence condition to a fluorescence one, and the content of cis-diols in the solution can be quantitatively evaluated with the fluorescence of obtained conjugate. In addition, there is a shift of the maximum absorption band of cis-diol derivate in the visible range. The scheme of ARS interaction with boronic acid is shown in figure 8.

In our work it is demonstrated with the formyl-furylboric acid and ARS in phosphate buffer
Figure 5. FTIR-spectra of furfurylborate (a) and $Fe_3O_4/3$-APS/furfurylborate nanocomposite (b).

Figure 6. Reaction of diols with phenyl-boronic acids.

Figure 7. Chemical structure of ARS dye.

(figure 9). A typical solution for the study of binding fluorescence dye ARS and boronic acids consisted of phosphate buffer at pH=7.4, ARS (0.01 mM) and boronic acid ranging in concentrations from 0.01 to 1 mM. ARS show acidic properties: $pK_{a1} = 5.5$; $pK_{a2} = 9.5$. 
Figure 8. Competitive binding of a Boronic acid with ARS and a 1,2-diol.

\[ \lambda_{\text{max}} = 515 \text{ nm (figure 9).} \]

Figure 9. UV-Vis spectra of ARS (a) and furfurylboronic acid/ARS conjugate (b).

The formation of ARS-\(Fe_3O_4/3\)-APS/furfurylboric acid conjugate occurs according to the scheme in figure 10.

After the chemisorption on boronfurfurol, the ARS molecule switches from a non-fluorescent to a fluorescent state. Immobilization of ARS on \(Fe_3O_4/3\)-APS/furfurylboration nanocomposite allows creation fluorescent probe on nanocomposite surfaces. In our work, it has been demonstrated by the formation of conjugate formylfurfuryl boronic acid with ARS in phosphate buffer (pH=7.4). A shift of ARS adsorption maximum from 515 nm to 425 nm in ARS-furfurylboric acid conjugate indirectly confirms changes in the electronic state of the ARS molecule, necessary for fluorescent state switching.

Based on published data [17], in case of the addition of carbohydrates in the form of cis-diol form the competitive replacement ARS on the surface of the composite to sugar molecules should
Recognition of different simple sugars in human blood is an important task for current medicine. The most promising way to construct fructose-sensitive materials is to use the ability of boronic acid to form reversible covalent complexes with 1,2- and 1,3-diols [16,18,19]. Boronic acids have relatively small toxicity and can be considered “green” compounds [16]. The release of ARS was confirmed by photocolorimetric method (λ = 440 nm). A model experiment was being conducted that based on competitive sorption phenomena between ARS at the surface of nanocomposites and fructose. It passes according to the scheme in figure 11.

**Figure 10.** Scheme of the interaction of ARS with boronic acid immobilized on the surface of magnetic Gd-containing particles.

**Figure 11.** Scheme of fructose interaction with ARS on the surface of boronic acid/magnetic Gd-containing particles.
We have estimated the amount of available boronic groups on the surface using a reaction composite with sugar. As it can be seen from figure 12, the amount of released ARS is proportional to the concentration of sugar in the added solution. The maximum amount of released ARS corresponds to the calculated boronic acid content of 1.76 mmol/g. Taking into account the number of amino groups in the initial composite (2.2 mmol/g), one can conclude that the immobilization efficiency for the boronic acid derivative is 80%. However, not all the boronic acids moieties on the surface can be available for the reaction with sugar due to steric hindrance.

![Figure 12. The optical density of sugar-containing solutions after reaction with boronic acid/magnetic Gd-containing particles bound with ARS.](image)

4. Conclusions
Aiming to develop new magnetic materials for neutron shielding applications, we have used a bottom-up approach for the synthesis of promising boron-containing nanocomposites on a \( \text{Fe}_3\text{O}_4/3-\text{APS} \) basis. Performed formation of \( \text{Fe}_3\text{O}_4/3-\text{APS/furfuryl boronic acid} \) conjugate with ARS which opened up the path for fluorescent determination of these kinds of nanocomposites due to inherent changes in the electronic structure of the dye adsorbed on the surface. Due to the presence of boronic acids on the composite surface, the composite changes the color of the sugar-containing solutions, allowing to control of the amount of immobilized boronic acid derivative.

We can propose the use of such multifunctional B/Gd-containing magnetic nanocomposites as a magnetic actuator membrane, providing efficient shielding “on-demand” maintaining strong interaction with neutrons. This work, we believe, is contributing to sustainable development goals 9 (industry and innovation) since it offers an innovative approach for neutron shielding and 12 (responsible production) due to the possibility to extract recycle such a magnetic material using strong magnetic field.

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