Synthesis and Evaluation of Types of Shells on Fe_3O_4 Nanoparticles by SPME Method for Determination of Ti (IV) in Toothpaste by Spectrophotometry Using Experimental Design

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ABSTRACT

Magnetic Solid Phase Microextraction (MSPME) was investigated as a safe, fast and inexpensive method to measure titanium element by the complex formation with 4-(2-Pyridylazo)-resorcinol as a ligand. First of all, the synthesized nanoparticles were coated with different shells including SiO_2, TiO_2, chitosan and active carbon. Then, the titanium adsorption cations were evaluated. The complex formation was measured via UV/Vis spectroscopy and the wavelength maximum absorption was determined at 520 nm. The optimization process was performed in two ways. First, eight parameters: pH, volume of aqueous phase (V_{aq}), sorbent amount (SA), organic solvent volume (V_{org}), adsorption time (t_{ads}), desorption time (t_{des}), salt amount (NaCl) and ligand concentration (LC) were optimized by Plackett-Burman Design (PBD) in statistical software package Minitab ver. 17.0. Secondly, some parameters values were investigated for more confidence by One Variable at a Time (OVAT) method. Finally, the results demonstrated that the best condition of absorption of titanium cations is: $Fe_3O_4@SiO_2$, acetonitrile as desorption organic solvent with 300 ml, volume and pH=3. The calibration curve was linear between 0.01 and 0.6 µg/ml with a detection limit of 0.003 µg/ml, and Relative Standard Deviation (RSD %)(N=5) for concentration of 0.2 µg/ml was 4.2%. This method was used for toothpaste sample and an acceptable percentage of relative recovery (78.6%) was obtained.

Key words: Resorcinol, Ti^{4+}, $Fe_3O_4@SiO_2$ nanoparticle, MSPME, experimental design.

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INTRODUCTION

The most common natural and stable form of TiO_2 is rutile and it is the primary source of titanium oxide. Titanium oxide has many industrial applications ranging from pigment, sun cream, paint and toothpaste to photovoltaics, photocatalysis photo/electrochromics and sensors [1]. Extraction of Titanium oxide has great importance due to its promising application and great value it. Khezri and coworkers, showed that extraction of titanium even in small quantities from sludge, is beneficial to factories and also aid in decreasing the environmental pollutant [2]. Extraction is the oldest, most applicable and also basic technique of sample preparation. This method requires that analyte in sample matrix is separated by a solvent so that the analysis process can be affected by minimum matrix interferences and matrix effects.

The Extraction principle is based on a selective transfer of one or more solute(s) in aqueous media to a solvent which is an immiscible organic liquid or one or more components in dissolved or suspended form in the liquid. The first procedure in which the solute partitions two immiscible phases is Liquid -Liquid Extraction (LLE) and second one is Solid Phase Extraction (SPE) [3]. Solid phase extraction was introduced into the market through Waters Co. in 1978 and sold in Sep-Pak. Although, SPE takes priority over LLE due to some features including being faster, requires less solvent, and is easily automatable, both solvent based extraction methods have less recovery [4]. Thus, there is a great tendency to replace liquid based extraction to reduce toxic

solvent, reduce analyte losses and sample manipulation.

Other developed methods, caused solventless or reduction of an organic solvent such as solid phase micro extraction. Solid Phase Microextraction (SPME) is used as a solvent-free sample preparation method. The main idea of this technique is to apply a small amount of extracting phase [5]. Stir Bar Sorptive Extraction (SBSE) was proposed in 1999 as an alternative to solid phase microextraction and lately, more advances were reported, but due to high cost, it is rarely used [6]. SPME evaluations are carried out under conditions of non-equilibrium; also, it needs quite large solid sorbents because it encounters rate diffusion limitation and mass transfer in bulk solid sorbent restriction. So, application of micro/nano size particles adsorbent could be a practical solution to removing these limitations by increasing the interfacial area of the absorbent [7]. Moreover, Nano-structure sorbents provide excellent qualities such as wide range of interactions; also, too many reactive sites which make them appropriate choice for extracting phase in dispersive microextraction technology [8]. Recently, Carbon based nanomaterials were functionalized by ionic liquid applied for sample preparation [9] such as graphene oxide nanoparticle that is used for chromatographic separation [10]. The mentioned qualities and features led to generation of new method in separation science and technology. The Magnetic Based Solid Phase Extraction (MSPME), covers necessity of loading of suspension on the SPE cartridge by dispersion in the sample matrix, producing higher mass transfer and direct contact with an analyte and selective adsorption [11]. Finally, an external magnet will separate magnetite nanoparticles from sample solute [12].

The adsorption layer may enhance resistance against oxidation of magnetite and help in grafting negative and positive ions [13]. To the best of the authors' knowledge, this is the first time that different types of shells are compared to determine the most capable coated agent for Ti^{4+} microextraction.

To optimize more than one variable at a time, multivariable strategy has been widely used to assess the influence of factors on MSPME results. Plackett-Burman Design (PBD) technique is one of useful and extensive multivariable method that is used to estimate the effect of factors [14-15]. This technology has been applied as a fast, economic, and effective method, and Faheem et al. have used this technology as a powerful chemometrics tool in microextraction [16].

The aim of this study is to apply new microextraction pathway to preconcentrate and determine titanium oxide in combination with Plackett-Burman Design (PBD) to optimize the effective parameters on magnetic solid phase microextraction, followed by UV/Vis Spectroscopy. These factors factors include pH, volume of aqueous phase (V_{aq}), sorbent amount (SA), volume of organic solvent (V_{org}), time of adsorption (t_{ads}), time of desorption (t_{des}), amount of salt (NaCl) and ligand concentration (LC). Moreover, some significant parameters were investigated on extraction of Ti (IV) efficiency using one variable at a time.

MATERIAL AND METHODS

Chemical and Reagent

High purity acid and reagent including,nitric acid (65percent), hydrochloric acid (35percent),methanol, ethanol, acetone,sodium hydroxide were purchased from Merck company (Darmstadt, Germany).Tetra Ethyl Ortho Silicate (TEOS) and (4-(2-Pridylazo –resorcinol)) and titanium oxide were purchased from Sigma Aldrich (Taufkirchen, Germany), Chitosan was obtained from Nano Rad Behan Gilan(Gilan, Iran).The TiO_2 stock standard solutions (100μg/mL) were prepared with addition of sufficient (10mg) amount of analyte in acidic media (mixture of HCl, H_2SO_4) and filling to mark line into 100 mL volumetric flask with deionized water. All other salts and reagents are purchased from Merck Company (Darmstadt, Germany).The Work solutions were prepared daily just before use by dilution of appropriate amount of stock solution.

Instrumentation

The ultra violet visible absorbance measurements of Ti (IV) were evaluated using UV/Vis spectrometer, with Xenon lamp and PDA detector (Varian Company, model Cary Bio 50, Australia) at maximum wavelength of 200 and 900 nm, respectively while, the identification of the present functional group was carried out via Fourier transform infrared spectrophotometer (FT-IR instrument model Bruker tensor ,Germany) using KBr pellets in the region, 400-4000cm^{-1} and (pH meter model 690 Metrohm ,Switzerland), also

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(Ultrasonic Bath model UP-100H Hielscher ,Germany), was employed for pH adjustment. Transmission Electron Microscopy (TEM) (Leo-912AB, Germany) was used to study morphology and size determination.

Synthesis and characterization

Synthesis of Nano Fe₃O₄: Nano-Fe₃O₄ was prepared using co-precipitation method of Seyedsadjadi and co-workers [17] with slight modification. Briefly, 1.4705 g trisodium citrate, 0.8 g sodium hydroxide and 17.04g sodium nitrate were dissolved in 90 mL deionized water. This mixture was heated to 100°C to obtain transparent solution. Next 10 mL of solution $FeSO_4.7H_2O$ 1 M was added to the resulting solution, shaken vigorously and kept at 100°C for 1 h. Following this, the precipitation was normally cooled down to room temperature, then separated by a magnet and washed with deionized water several times. Resultant black magnetic nanoparticles were dried at 60°C for 6 h under vacuum.

Synthesis of Nano Fe₃O₄ /SiO₂:Fe_3O_4-SiO_2 structures were prepared by Stober process [18]. This method is based on sol-gel method. 0.5g Fe_3O_4 nanoparticle was scattered by sonication in solution containing 80 mL ethanol and 20 mL distilled water for 30 min. Next, 5 mL NH_3 solution (28 w/w %) was added to 4 mL TEOS continuously. The resultant suspension was mixed and allowed to react at a room temperature for 6 h. The given core-shell Fe_3O_4-SiO_2 was obtained by magnet and washed with distilled water three times. Finally, this precipitate was dried at 60°C for 8 h under vacuum.

Synthesis of nano-Fe₃O₄-TiO₂: For preparation of Fe_3O_4-TiO_2, Nemati and colleagues [19], previously reported method was used. A certain amount of nano Fe_3O_4 particles was dispersed in a mixture of solvent, 250 mL of absolute ethanol, 90 mL acetonitrile and were sonicated for 15 min. Subsequently, 1.5 mL of aqueous NH_3 solution (25 wt.%) was added to it and stirred for 30 min. Afterwards, 3 mL of tetrabutyltitanate (TBOT) was dissolved in 20 mL of absolute ethanol and was added drop-wise to the solution while stirring at 30°C for 1.5 h. The resultant nanoparticle was collected, then washed three times with ethanol and dried at room temperature.

Synthesis of nano-Fe₃O₄-Chitosan

To synthesize these nanoparticles, the modified method of Molhotra and co-workers [20] was used. For preparation of 5% chitosan, 50 mg of chitosan was dissolved in 100 mL acetate buffer (0.05 M, pH 4.2) solution and the obtained solution was sonicated for 30 min. Following this, 0.1 g Fe_3O_4 nanoparticles were dispersed in 10 mL of the chitosan solution by stirring at room temperature and highly viscous homogenous solution of chitosan with nanoparticles was obtained, also NaOH 1 M was added to it during the stirring process and the condition of stirring remained constant for 15 min. The nanoparticles were isolated due to the strong magnet, as a result, the supernatant solution was discarded. Furthermore, the resultant nanoparticles were washed several times with acetate buffer pH=4 in the main wheil, 10 mL deionized water was added and 2 mL of glutaraldehyde was used to establish crosslinks. Ultimately, the solution was stirred for 12 h by vortex and nanoparticles were accumulated, and washed, then placed in a desiccator until it was dry.

Synthesis of nano-magnetic-active carbon

First, active carbon was purified by using concentrated HCl at room temperature and the modified active carbon was sonicated for 40 min. Hereupon, the given sample was filtered and washed 3 times with deionized water and then the purified carbon was dried. In the next stage, to modify active carbon, a certain amount of active carbon was refluxed for 24 h in nitric acid (30 %). The mixture was then filtered by Buchner funnel and washed several times, so that it could be heated in an oven. In the final stage, 10 g of modified active carbon was mixed with 1 g of Fe_3O_4 nanoparticles, sonicated for 4 h, and then dried in oven at 100 °C. The next mixture was placed in desiccator until used.

Magnetite based solid phase microxtration

First, the stock solution of titanium oxide was prepared with solvation of 0.1 g TiO_2 in concentrated HCl and hot H_2SO_4 and balloon was filled to volume of 100 mL with distilled water. Other solutions were prepared from dilution of stock solution, daily.

The titanium aqueous solution at concentration of 0.1 μg/ml and the ligand solution containing (4-(2Pridylazo –resorcinol)) at concentration level of 30 μg/ml, were prepared by dissolving in water and the final solution was obtained from Ti^{+4} solution, then the pH value of the solution was adjusted to the desired pH using 0.1mol/L HCl and 0.1 mol/L NaOH. The desired amount of different

absorbents: Fe3O4, Fe₃O₄@SiO₂, Fe₃O₄@chitosan,and Fe₃O₄@TiO₂ were added to the solution. Subsequently, ultrasonic was applied for about 5 min to obtain a better dispersed mixture and the supernatant solution was discarded. After sedimentation of loaded particles, an external magnet field was used to separate the absorbent. Hereupon, the loaded MNPs were eluted by appropriated amount of solvents (acetonitrile, methanol, nitric acid + methanol, nitric acid and methanol + water) and adsorb analytes were desorbed. Following this, the sonication process led to mixture of the solution and assisted in transferring mass between the organic media and nanoparticles. Next, the liquid phase was collected and added to the ligand solution to form a complex. Finally, the obtained complex was transferred to UV/Vis microcell and the absorbance at maximum wavelength, 520 nm, was measured. Equations (1), (2) and (3) were used to calculate Enrichment Factors (EFs), Preconcentration Factor (PF), Relative Recovery (RR%), Extraction Recovery (Re%), as well as under study procedure[21,22].

$$EF = \frac{A_{after\ extraction}}{A_{before\ extraction}} \text{Eq. (1)}$$

$$PF = EF \times \frac{V_{solvent}}{V_{nanoparticle}} \text{Eq. (2)}$$

$$RR\% = \frac{C_{founded} - C_{real}}{C_{added}} \text{Eq. (3)}$$

The calibration curve was obtained from different cation solutions, ranging from 0.001 to1 μg/mL and to estimate the efficiency of MSPME analytical figure of merit enrichment factor, relative recovery was calculated.

Experimental design
 The aim of this study was to consider the significance and optimization of eight parameters in Ti extraction; in order to reach this goal, Minitab software version17 was applied as a powerful experiment design and optimization tool. However, some variables were optimized via classical one variable at a time method.

The Plackett-Burman design (PBD) was used to show the importance of variables through few experiments. This means only 15 runs were launched and the most optimum values of factors were gained; while on the other hand, with full factorial design, in order to estimate the effect of all variables, more experiments were required (2^8=256).

As a 2 level design experiment method, each estimate variable including: pH (A), volume of aqueous phase (V aq) (B), sorbent amount (SA) (C), volume of organic solvent (V org) (D), time of adsorption (t ads) (E), time of desorption (t des)(F), amount of salt (NaCl) (G) and ligand concentration (LC) (H) had high (+) and low (-) effect on extraction efficiency. The parameters with confidence level of more than 90% and p value < 0.01 in Pareto chart had significant influence on microextraction efficiency.

RESULTS

Characterization of synthesis nanosorbent Sorbent characterizations by FTIR spectroscopy
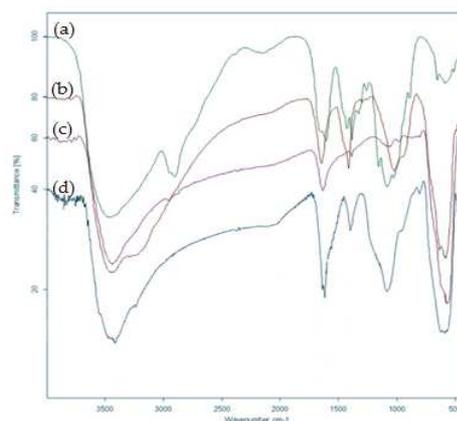
Figure 1: (a) FT-IR spectra of Fe₃O₄ @chitosan (green color); (b) FT-IR spectra of Fe₃O₄@TiO₂ (brown color); (c) FT-IR spectra of Fe₃O₄ nano-particles (purple color); and (d) FT-IR spectra of Fe₃O₄@SiO₂ (blue color).

As shown in Figure 1, pure Fe₃O₄ nanoparticles (purple color graph) has 4 main bands in the spectrum. The bands at 582.38, and 1627.79 cm⁻¹, correspond to Fe-O, O-H band bending vibration and 1066.07, and, 3490.57 cm⁻¹ are attributed to O-H stretching vibration, representing free or adsorbed water and OH groups cover the magnetite surface. Silica coated Fe₃O₄(blue line) characteristic adsorption appears as different bands as follows. The Fe-O magnetite band representpeaks under 600 cm⁻¹ and a sharp bond at 466.64 cm⁻¹correspondto bending vibrations of Si-O-Si or O-Si-O bond mode,

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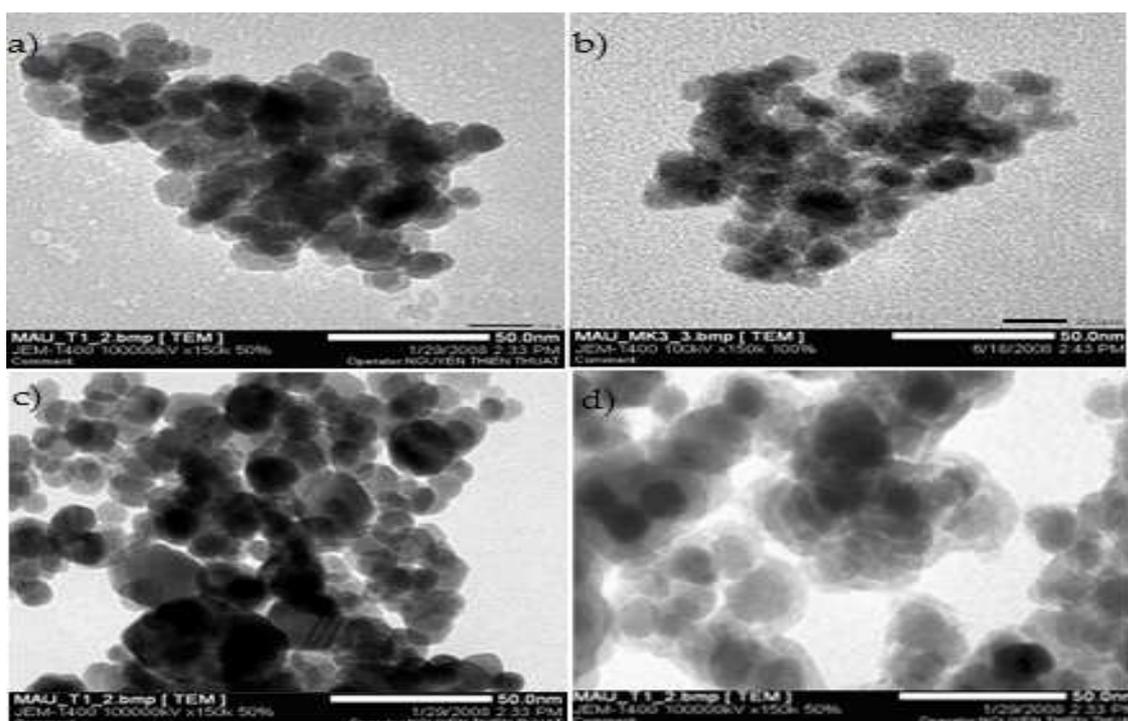
Figure 2: TEM images of synthesis of nanoparticles: a) Fe$_3$O$_4$;b) Fe$_3$O$_4$-chitosan; c)Fe$_3$O$_4$-TiO$_2$; d)Fe$_3$O$_4$-SiO$_2$

while the band with high intensity at 1084.70 cm^{-1} is assigned to asymmetric stretching band of Si-O-Si and Fe-O-Si bonds also, and due to observation of O-H, a broad band of over 3400 cm^{-1} can be seen [23-25].

The FT-IR spectrum of Fe$_3$O$_4$ @TiO$_2$ (brown color) in Fig. 1 demonstrate a broad peak at 700-500 cm^{-1}, which is ascribed to the vibration of the Metal-O functional group. The peak at 582.24 cm^{-1} can be assigned to the vibration of the Fe-O functional group. Ti-O absorption peak appeared at 466.19 cm^{-1} and may also overlap to 582.24 cm^{-1}. The peak appearing at 1402.25, and 1017.04 cm^{-1} can be associated with the presence of stretching vibrations of Ti-O and Fe-O-Ti bonds. The band at 1631.33 cm^{-1} belongs to the H-O-H bending vibration, indicating OH group presence in nano-Fe$_3$O$_4$-TiO$_2$.

In the IR spectrum Fe$_3$O$_4$@Chitosan (green color) in Fig. 1, five bands at: 3417.51, 1601.11, 1423.45, 1383.57 and 1086.54 cm^{-1} can be seen. The band at 3417.51 cm^{-1} corresponds to stretching vibrations of the O-H bond and NH$_2$ group. The bond at 1601.11 cm^{-1} corresponds to vibrations of the N-H bond in NH$_2$. The bond at about 1423.45 cm^{-1} is due to stretching vibrations of the C-N bond and bond at 1383.57 cm^{-1} is because of deformation N-H in NH$_2$. The bond at 1086.54 cm^{-1}

is specified for stretching vibrations C=O in C-OH. All the basic functional groups in chitosan can be viewed in IR spectrum.

Characterization of synthesis nano-sorbent by TEM
Study of morphology and size of synthesis nanoparticles are done by tunneling electron microscopy. As shown in Fig. 2, in the 4 images, nanoparticles are synthesized very well. Estimated average size for each particle is about 20-30 nm.

Optimization process
Optimization by Experimental design method
The main feature of fractional factorial design such as Plackett-Burman Design (PBD) in comparison with full factorial design is the lack of interaction between the parameters, resulting in the lower number of experiments. Yet, this statistical design of experimental method can be employed to optimize variables, screen and identify the significant factors [24].

Plackett-Burman experiment design technique shows the impact of eight variables through 15 runs, on micro extraction which were investigated, and the obtained result at 90% confidence level (p≤ 0.01) was visualized by Pareto chart. Pareto chart is used to determine the magnitude and

importance of an effect. The chart displays the absolute value of the effects and draws a reference line on the chart. Any effect that extends or passes this reference line is statistically significant.

As shown in Fig. 3 the vertical standardized effect line value with 2.015 is the significant criterion for each parameter, contributing to extraction efficiency. When each term exceeds the line, it means the corresponding variable can be considered as significant factor. Here, the only important parameter is volume of organic solvent (V_{org}) while, the other terms such as A, B, C, E, F, G, and H are non-significant terms. As previously mentioned, the amounts and levels of the factors (low (−) and high (+)) are considered (Table 1). Furthermore, Placket-Burman design was carried out by eight factors, containing 15 runs, and the PB experimental design matrix and the analytical response (absorbance) for each run is shown in Table 2.

Estimating the influence of several variables which also demonstrate the effect of each exprimental setting to predicting response the optimization plots that are drawn. After fitting a model, the reponse optimizer can be utilized and this must be done for each respose independently.

Depending on the conditions ,dectating to the optimazation tool, the optimal response was created. Then the desirability and the weight of each parameter was calculated. The obtained values are used to evaluate the desirability of the multiresponse system. The column represents the impact of each variable, while the row is showing the response; where as the red lines are current values of parameters. Here, the highest absorbance or extraction efficiency condition occurred when the variable has the values shown
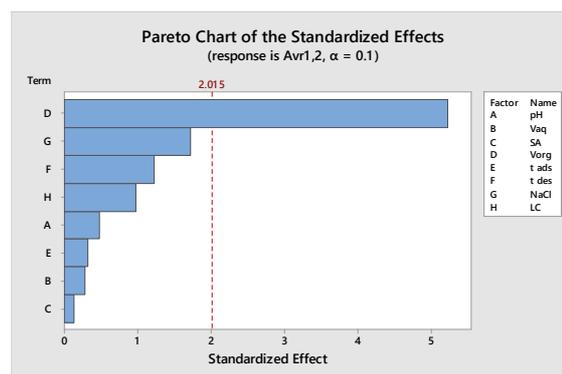
Figure 3: The standardized main effect Pareto chart for PBD.

Table 1: The experimental range definition for PBD

Variables	Symbols	Low(-)	High(+)
pH	pH	3.0	9.0
Volume of aqueous solution(mL)	V_{aq}	5.0	15
Amount of sorbent (mg)	SA	10	50
Volume of organic solvent (μL)	V_{org}	300	700
Time of adsorption(min)	T_{ads}	10	30
Time of desorption (min)	T_{des}	5.0	15
Amount of salt (%W/V)	NaCl	0.0	2.0
Ligand concentration (μg/mL)	LC	80	120

Table 2: The results of Placket-Burman experimental design matrix

StdOrder	RunOrder	pH	V_{aq}[mL]	SA[mg]	V_{org}[μL]	t_{ads}[min]	t_{des}[min]	NaCl [w/v%]	LC [μg/mL]	Abs
11	1	3.0	15	10	300	10	15	2.0	120	0.293
7	2	3.0	15	50	700	10	15	2.0	80	0.077
14	3	6.0	10	30	500	20	10	1.0	100	0.168
5	4	9.0	15	10	700	30	5.0	2.0	80	0.156
3	5	3.0	15	50	300	30	5.0	0.0	80	0.319
10	6	9.0	5.0	10	300	30	15	2.0	80	0.205
2	7	9.0	15	10	700	10	5.0	0.0	120	0.175
8	8	3.0	5.0	50	700	30	5.0	2.0	120	0.180
13	9	6.0	10	30	500	20	10	1.0	100	0.174
12	10	3.0	5.0	10	300	10	5.0	0.0	80	0.275
1	11	9.0	5.0	50	300	10	5.0	2.0	120	0.253
9	12	3.0	5.0	10	700	30	15	0.0	120	0.164
4	13	9.0	5.0	50	700	10	15	0.0	80	0.182
6	14	9.0	15	50	300	30	15	0.0	120	0.274
15	15	6.0	10	30	500	20	10	1.0	100	0.164

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in Table 3.The optimal chart of PBD for examined factors was obtained as displayed in Fig. 4.

Figure 4: The optimal chart obtained from PBD

Analysis of regression generated an equation, to describe the correlation between response and predictors, and this equation is used to model and determine the mentioned relationship. The outcomes of regression analysis show statistically, the significant relationship between response and predictors.

The following equation showed an empirical relationship between response and input variables in uncoded values. Empirical models are generated in terms of uncoded (actual) factors as in Eq. 4.

Regression Equation in Uncoded Units:

$$Abs = 0.3439 - 0.00176\,pH + 0.00060\,V_{aq} + 0.000069\,SA - 0.000285\,V_{org} + 0.00035\,t_{ads} - 0.00269\,t_{des} - 0.0188\,NaCl + 0.000528\,LC \quad \text{Eq. (4)}$$

An ANOVA was used to verify whether the main effects are significant. A p-value less than 0.05 in the ANOVA table shows the statistical significance of an effect at 95% confidence level. In this work, a p-value less than 0.01 indicates that the factor is statistically significant. In table 4, only volume of organic solvent (V_{org}) is significant, as shown in Fig. 2 (Pareto chart).

Optimization by one-variable at a time method
In the next stage, to ensure accuracy of the method, under study, some important parameters were investigated by one-variable at the time method. In one variable ata time (OVAT) method, one parameter is varied while the others maintain fixed.

Optimization of type of nanosorbent
Nanoparticles with different types of shell such as TiO_2, chitosan, SiO_2 and active carbon were used. As shown in Fig. 5, in comparison with other nanoparticles core shells the silica coating Fe_3O_4 has the greatest efficiency. This may result from sorption capacity, depending on factors, such as pH, active site number, electrostatic interactions between sorbent and Ti^{4+}, and surface charges. The pH has great impact on sorption capacity, with respect to the adsorption of different types of ions onto oxide surface.This parameter results in distribution of active sites on Fe_3O_4 with SiO_2 coated layer and better bending with Ti^{4+} due to hydroxyl groups. In addition, with the low pH range (pH<3) the non-coated Fe_3O_4 is rarely stable and undergoes decomposition and as a result, it has the lowest sorption capacity.

Table 3: Optimum amounts of parameters based on PBD.

Factor name	pH	V_{aq} [mL]	SA [mg]	V_{org} [µL]	T_{ads} [min]	T_{des} [min]	NaCl [W/V%]	LC [µg/mL]
Optimum amount	3.0	15	50	300	30	5.0	0.0	120

Table 4: Analysis of variance table (ANOVA) for PBD.

Source	DF	Adj SS	Adj MS	F-Value	P-Value
Model	9	0.051964	0.005774	4.05	0.069
Linear	8	0.047295	0.005912	4.15	0.067
pH	1	0.000333	0.000333	0.23	0.649
V_{aq}	1	0.000108	0.000108	0.08	0.794
SA	1	0.000023	0.000023	0.02	0.904
V_{org}	1	0.038947	0.038947	27.3	0.003
t $_{ads}$	1	0.000147	0.000147	0.10	0.761
t $_{des}$	1	0.002166	0.002166	1.52	0.273
NaCl	1	0.00423	0.00423	2.97	0.146
LC	1	0.00134	0.00134	0.94	0.377
Curvature	1	0.004669	0.004669	3.27	0.130
Error	5	0.00713	0.001426		
Lack-of-Fit	3	0.007072	0.002357	81.5	0.012
Pure Error	2	0.000058	0.000029		
Total	14	0.059094			

In the case of $Fe_3O_4@TiO_2$, the isoelectric point occurs at 6.2, meaning it is covered by dense positive group, generating electrostatic repulsion between sorbent and the cation [26]. Amino groups can easily chelate with Ti^{4+} via amino groups, presented on the surface of chitosan. Amino groups are larger functional group than hydroxyl; so, the density of negative surface charge seems to be fewer than $Fe_3O_4@SiO_2$; consequently, chitosan coated particles has less active site and finally less extraction efficiency. Magnetite nanoparticles with active carbon coating have few numbers of functional groups per surface unit. Furthermore, the density of functional group depends on the precursor's nature and condition of preparation [27]. Thus, the coated nanoparticles with active carbon have less tendency to absorb Ti^{+4} in compare to other nano sorbents, applied in this investigation. In conclusion, with respect to all points mentioned above, $Fe_3O_4@SiO_2$ particle is a unique sorbent for titanium microextraction.
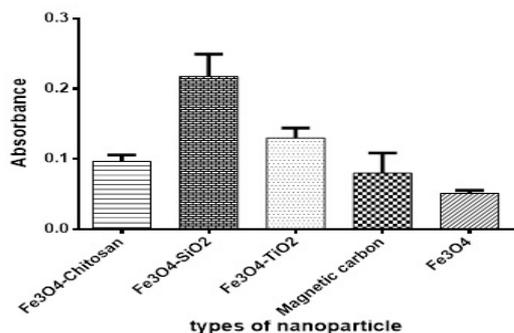
Figure 5: The effect of types of nanoparticle on the extraction efficiency of Ti⁴⁺

Optimization of type of desorption solvent

To obtain better interaction with target analyte, and organic eluents are widely used due to their functional group and their polarities. Typically, in dispersive microextraction eluents with high density such as chlorobenzenes and CS_2 are applied;however, in recent years, micro extraction with low-density solvent, hexyl acetate 1-octanol was reported [28]. According to the present investigation, the best choice among acetonitrile, methanol, nitric acid and water is acetonitrile. The high polarity of acetonitrile causes the state of superiority in this organic solvent to other eluents and also better solubility of Ti^{4+}, excellent extraction. Thus, it is selected as an organic solvent for further experiments (Fig. 6)
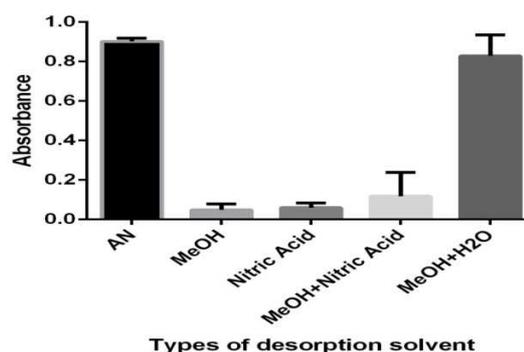
Figure 6.The effect of types of desorption solvent on the extraction efficiency of Ti⁴⁺

Optimization of volume of desorption solvent

The effect of extraction solvent on the extracted cation and performance of the procedure was studied in the range of 200-700 μL. Fig. 6 presents the variation of absorbance versus volume of desorption solvent, and as shown, the absorbance increases slowly until 300 μL and it decreases slightly from approximate 0.7 to around 0.4, when the eluent volume rises.
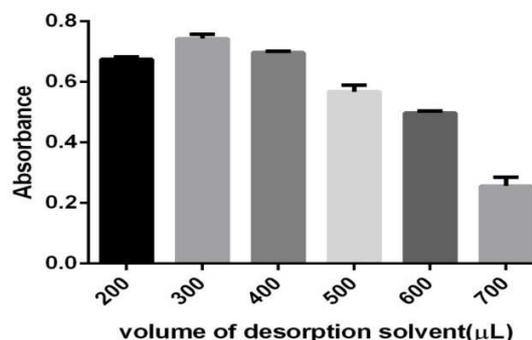
Figure 7: The effect of volume of desorption solvent on the extraction efficiency of Ti⁴⁺

Optimization of pH

pH plays an important role in the extraction process and for Ti^{+4}extraction, the best condition of extractionis occurred in the acidic media. The impact of pH was investigated in the range of 2 to 9 and as the outcomes indicated in Fig. 8, the best pH is 3. So, the pH for better extraction performance was 3, which was selected for subsequence studies. In addition, the negative surface charge of silica coated nanoparticle results in ion pair formation with Ti^{+2} and consequently, superior molecular attraction. So, this study was carried out at pH = 3.
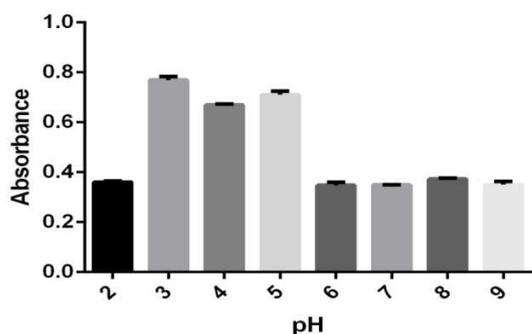
Figure 8:The effect of pH on the extraction efficiency of Ti⁴⁺

Calibration Curve

A series of samples (10) ranging from 0.001 to 1.000 μg/ mL were selected to establish a calibration curve and the obtained data is presented in Fig. 9. The figure indicates that there is a linear response at the beginning of graph until 0.6 μg/mL with correlation coefficient (R^2=0.9889), showing a good applicability of the method for cation quantification.

$$y = 2.7508x + 0.0229$$
$$R^2 = 0.9894$$
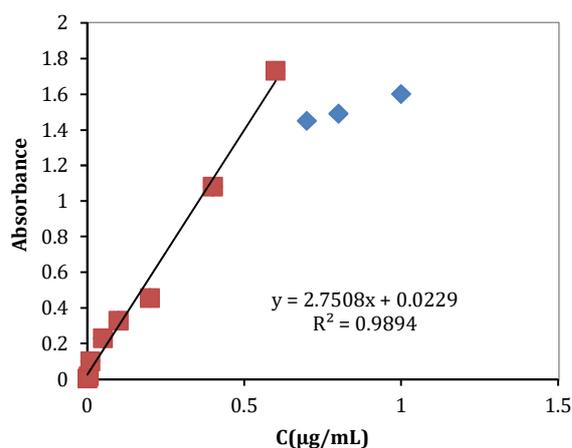
Figure 9: Calibration curve in optimal condition for extraction of Ti⁴⁺

Analysis of figure of merit

The standard solutions were prepared with distilled water to calculate the practical application of the nano structures based on SPME. Thus, Limits Of Detection (LODs), linear dynamic range (LDRs), limit Of Quantification (LOQs), reproducibility, repeatability, Relative Recovery (RR%), Pre-concentration factor (PFs) and Enrichment Factor (EFs) were determined. Pre-concentration factor is a ratio of concentration between acceptor phase and initial donor phase aqueous solution. For the determination of this factor, the absorbance peak after extraction of 0.6 μg/mL analyte was divided into absorbance peak

before extraction the same conditions of multiplied dilution factor. After extraction of the analyte into nanoparticles, it was desorbed with 300 μL of acetonitrile. The volume of donor phase was 15 mL. Dilution factor was calculated as 15/0.3 = 50. The pre-concentration factor (PF) and enrichment factor (EF) were calculated and were equal to 386, 7.72, respectively based on equations 2 and 3. The calibration curve at 520 nm wavelength had linear response between 0.001 and 0.6 (μg/ml) with coefficient determination (R^2) 0.9889. The two key parameters LODs and LOQs, are 0.0019 and 0.0065 μg/ml respectively, yielding signal to noise ratio. Repeatability (RSDs, n=5 sample at 200 μg mL^{-1} level of the analytes 4.2) was obtained under optimal condition of the study.

Study of interferences

Every sample has many constituents and they may have significant impact on the extraction procedure. The aim of the interferences study is to determine and examine of method's selectivity when interferences exist. For this goal, certain amount of solution containing corresponding cation in the presence of different contaminating ions was treated based on the suggested method and the results are shown in Table 5. These digits indicate plainly, that magnetite based microextraction can be an applicable method to determine Ti⁺⁴.

Study on the validity of the method by real sample.

Preparation of ore samples

The accuracy and applicability of the proposed method were demonstrated by the determination of Ti (IV) in toothpaste samples obtained from different company in Iran. Five-gram weights of the samples were dried at 90° C for 2 h, ground mixed with 10 mL of concentrated HCl, 2 mL of concentrated HNO_3 and heated on a hot plate to dissolve. Finally, 20 mL of H_2SO_4 (1:1 v/v) was added, and the solution was cooled. The titanyl sulfate solution left was then properly hydrolyzed with ammonia, calcined, and crystallized; producing high-quality white TiO_2. After filtration and washing with deionized water, TiO_2 was dissolved in sulfuric acid and this solution was brought to a final volume of 250 mL with deionized water. Five milliliter aliquots of the final clear solution were analyzed by the prescribed procedure.

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Table 5: Effect of interferences on determination of Ti⁴⁺

	RR% in 0.1[μg/mL]	RR% in 1 [μg/mL]
$NaNO_3$	90	89
$Ca(NO_3)_2$	65	51
$Co(NO_3)_2$	45	32
$Cr(NO3)_3$	75	55
$Ni(NO_3)_2$	58	55
$Mg(NO_3)_2$	96	91
$Al(NO_3)_3$	94	90

Table 6.Related digit for study of real sample

Matrix	C_a [μg/mL]	C_f [μg/mL]	RR%	RSD
Toothpaste	0.000	0.002	-	4.60
	0.200	0.175	87.6	4.20
	0.500	0.456	91.3	5.59

C_a=add; C_f=Found

The proposed methodology was employed to determine and evaluate the validity of the obtained optimized condition. So, the real sample (toothpaste ash) was examined and the results show the validity of the proposed developed method (Table 6).

CONCLUSIONS

In the current, the optimization of magnetite nanoparticles based microextraction using statistical software (Mini tab) in combination with UV/Vis spectrophotometry for Ti⁺⁴in real sample was performed for the first time. Several core shell nano sorbents were synthesized and among them $Fe_3O_4@SiO_2$ had the best sorption capacity and it was successfully used for microextraction of Ti+4. Quantitative determination of titanium by magnetite based microextraction(MSPME)is known as a fast, feasible, safe, solvent free, and low cast method, and all these advantages has made scientists to pay more attention to this technique. The combination of this separation technique with statistical experiment design (software) transform microextraction to a time saving method due to minimization of experiments number. Two methods were employed to design the experiments. Firstly, Plakett-Burman design model and then to gain better accuracy confidence one variable at a time (OVAT) were used. Nevertheless, Plakett-Burman design model was used to evaluate the impact of eight variables on relative recovery was in the range of 87-91% at optimized condition. The real samples absorbance values were calculated for before and after extraction and average RSD% for water sample was suitable. It is shown that relative recovery for real sample was acceptable and the reported LOD is very low (0.0019).The results show that the only significant factor is the type of organic solvent and the proposed method has good accuracy and sensitivity.

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