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Spectrophotometric Determination of Naproxen using Chitosan Capped Silver Nanoparticles in Pharmaceutical Formulation

A. Barazandeh[a], G. D. Najafpour[b], A. Alihosseini*[a], S. Kazemi[c]

[a] *Department of Chemical Engineering, Central Tehran Branch, Islamic Azad University, Tehran, Iran*
[b] *Faculty of Chemical Engineering, Babol Noshirvani University of Technology, Babol, Iran*
[c] *Department of Pharmacology and Physiology, School of Medicine, Babol University of Medical Sciences, Babol, Iran*

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ABSTRACT

Naproxen (NP) is a non-steroidal anti-inflammatory drugs (NSAIDs) are widely used for the treatment of acute to chronic pain. The aim of this work was to develop a new, simple spectrophotometric method for determining the concentration of naproxen in pharmaceutical formulations by chitosan capped silver nanoparticles. The morphology and structure of the chitosan capped silver nanoparticles were determined by ultraviolet spectroscopy (UV), Fourier transform infrared spectroscopy (FT-IR), atomic force microscopy (AFM), dynamic light scattering (DLS) and zeta potential (ZP) under optimal conditions. The results showed that, synthesized chitosan capped silver nanoparticles were approximately with particle size of 100 nm poly dispersity index (PDI) 0.385 and strong anionic (-24.8mV) zeta potential at acidic condition. It was found that chitosan as a chiral selector was able to detect naproxen at optimal conditions. The method was successful to determine naproxen in drug tablets formulation. A relative standard deviation of 1.0% was determined for the analysis of naproxen in real samples. Validation of this method, including limit of detection and limit of quantification were accurately confirmed according to ICH instructions. Based on this method, the limit of detection (LOD) and the limit of quantification (LOQ) of naproxen were calculated 0.022 and 0.066 $molL^{-1}$, respectively. Analysis of statistical data, the reproducibility and accuracy of this method demonstrated that the use of this novel method is valuable and practical for determination of naproxen in pharmaceutical formulations.

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1. INTRODUCTION

Naproxen [(S) -2-(6-methoxy-2-naphthyl) propionic acid (Figure 1) is a chiral and nonsteroidal anti-inflammatory (NSAIDs) drug. Because of the (S)-naproxen isomer has just the favorable therapeutic effect; it is used in purest form for the treatment of diseases [1]. Naproxen is white and odorless powder, that is practically insoluble in water at low pH, but it can be soluble in water at alkaline condition (pH >8) [2]. It is an important member of the family of 2-aryl propionic acid derivatives; which commonly used for reducing moderate to severe pain, fever, inflammation, and stiffness owing to arthritis, gout, injury (such as fractures), tonsillitis and bursitis. It has also recently been reported that naproxen is effectively used in preventing the progression of bladder cancer [3]—Naproxen inhibits COX-1 and COX-2 enzymes can prevent the biosynthesis of prostaglandins [4]. Naproxen (NP) is widely used to treat acute to chronic pain most commonly in veterinary and human medicine because it is available without a prescription. Clinical and pharmacological analysis of this drug requires effective analytical measures for quality control. As well as recent overuse of naproxen has led to the classification of naproxen as an emerging contaminant in wastewater [5]. Therefore, finding a new accurate and fast economic identification method can be the answer to this problem to improve the cognition process. In order to determine naproxen in diagnostic laboratories, several analytical methods have been reported in the scientific

*Corresponding Author Institutional Email: Afsharalihosseini@iauctb.ac.ir (A. Alihosseini)

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literature such as spectrophotometry [6], electrochemical [7], high-performance liquid chromatography (HPLC) [8], etc. It can be mentioned that, HPLC method are highly accurate and sensitive in compared to other methods, but it is too expensive and time-consuming. Among the above methods, spectrophotometer is considered as the usual analytical method, due to its simplicity, availability, fast and low cost [9]. For that reason, a novel UV-spectrophotometric method for determining the amount of naproxen in tablets has been investigated. In this work, we developed a new, simple and economical spectrophotometric method for quantitative determination of concentration of naproxen in pharmaceutical formulations. There are number of investigations on spectrometric method for determination of naproxen. Maheshwari et al. [10] have examined a, simple UV-spectrophotometric method for determining the amount of naproxen tablets using niacinamide as hydrotropic solubilization additive. Mahmood et al. [11] have described a method for detecting the amount of naproxen in commercial tablets. In this method, first naproxen after modulation reaction to hydroxyl analog and then oxidation using potassium permanganate as an oxidant in an acidic environment, in commercial tablets was determined. Sastry et al. [12] have developed a spectrophotometric method to quantify naproxen. In their methods, naproxen was methylated to produce a color oxidative bonding with Gibb reagent in neutral phosphate buffer. Later on, Sastry et al. [13] have described another approach of spectrophotometric method based on the formation of a dye species with MBTH via oxidation of Ce (IV) or Fe (III) to determine naproxen. Pendari et al. [14] have examined the amount of naproxen in human plasma using spectrophotometry; in this approach, the non-ionized form of the drug with pure diethyl ether was extracted having yield of 94.6% and then naproxen was determined by measuring the peak amplitude in the second-order derivative spectrum at 328.2 nm. In this method, the amount of LOQ base on IUPAC was 2.42 μgmL^{-1}. Then, Khan et al. [15] have used 1-naphthylarnin and sodium nitrite to determine naproxen using spectrophotometer at wavelength of 480 nm. Duymus, et al. [16] have examined naproxen-induced complex with tetracyanoethyl ethane (TCNE), 2,3-dichloro-5,6-deciano-p-benzoquinone (DDQ), and p-chloranyl using a spectrophotometric device but its reagent was stable only for duration of five minutes. Alizadeh et al. [17] have described two spectrophotometric methods for determination of naproxen. These methods included the formation of ion pair complex with green bromocresol at 424 nm in the first method and the formation of aqueous bromothymol ion pair complex at 422 nm in the second method. Mahmood et al. [11] had proposed a new spectroscopic method which naproxen changed to hydroxy analog. They proposed a new spectroscopic method based on naproxen to hydroxy analog to determine naproxen. The modified compound was paralyzed using alkaline acid. In this approach, the limit of detection and the limit of quantitation were reported to be 0.0098 $\mu g \cdot mL^{-1}$and 0.03296 $\mu g \cdot mL^{-1}$, respectively. However, this method was much faster and easier than previous methods. In another investigation, Tashkhourian et al. [18] have explored spectrophotometric method based on silver nanoparticles with starch coating to determine naproxen which had limit of detection of 2.7×10^{-6} M. The objective of present work was to develop a fast spectrophotometric method using a new reagent of chitosan -capped silver nanoparticles for the detection of naproxen. Chitosan is a natural active polysaccharide derived from chitin. The excellent properties of chitosan such as biodegradability, biocompatibility, non-toxic, antibacterial and hydrophilic properties make it a good choice for enantiomer detection [19]. The amino groups in chitosan are important sites that can be used to synthesize metal nanoparticles [20]. In this regard, silver and gold nanoparticles are highly regarded by chemists due to their unique spectral and optical properties [21]. Gharibshahian [22] have investigated that the size, shape and structural quality of nanoparticles can affect their properties. These parameters are controlled by growth kinetics. The physical, optical, surface and size of nanomaterials make them attractive case study for exploring a new research field. Chitosan-capped silver nanoparticles are silver-based nanoparticles which is noticed as a group of structural and biological materials [9]. The proposed method is valuable for exact identification and quantification of the naproxen.

2. EXPERIMENTAL

2. 1. Materials Racemic naproxen and S- naproxen were purchased from Alborz Balk and Tehran Daru company, respectively. Silver nitrate ($AgNO_3$), sodium borohydride ($NaBH_4$), acetic acid (CH_3COOH), citric acid, sodium hydroxide and sodium citrate were purchased from Merck (Darmstadt, Germany). Chitosan was supplied by Sigma-Aldrich company (St. Louis, Mo, USA).

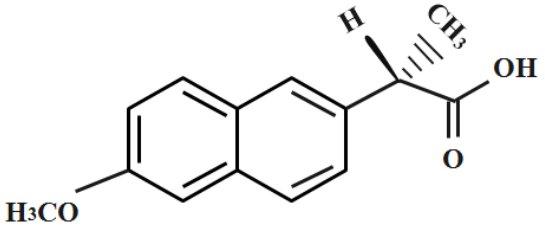

Figure 1. Chemical structure of naproxen

2. 2. Apparatus Chitosan-capped silver nanoparticles were measured by spectrophotometer UV VIS model SPEKOL 1500 Analytik Jena AG; Fourier transform infrared (FT-IR) spectra were analyzed using KBr pellets by a FT-IR spectrometer (WQF - 510A, China). In addition, atomic force microscopy (AFM) model easy scan 2 (Liestal, Switzerland), dynamic light scattering (DLS) and zeta potential (HORIBA - SZ100), were used to characterized nanoparticle.

2. 3. General Procedure To determine naproxen, chitosan-coated silver nanoparticles were first synthesized. Morphology and structure of chitosan-coated silver nanoparticles using ultraviolet (UV) spectroscopy, Fourier transform infrared spectroscopy (FT-IR), atomic force microscopy (AFM), DLS (dynamic light scattering) and ZP (zeta potential) were determined under optimal conditions. Using silver nanoparticles coated with chitosan, the amount of naproxen was determined by spectrophotometry in tablets.

2. 4. Synthesis of Chitosan Capped Silver Nanoparticles Using a method by reducing $NaBH_4$ from $AgNO_3$ in the presence of chitosan, with slight modification according to the previously reported method [23], silver nanoparticles capped with chitosan (Ag NPs) were synthesized. In the first step, 25 mg chitosan was dissolved in 50 mL of 4% aqueous acetic acid and then sonicated for 5 min. In the second stage, 20 mL of the solution was mixed with 50 mL of aqueous $AgNO_3$ solution (6 $mmol.L^{-1}$) and reaction was performed at room temperature under vigorous magnetic stirring for 30 min. In the third stage, a freshly prepared aqueous solution of $NaBH_4$ (1 mL, 58mmol. L^{-1}) was added dropwise to the reaction mixture. After stirring with a magnetic stirrer for 2 hours, observing the color change of the solution to yellowish brown is a sign of synthesis (Ag NPs) in the solution. By increasing the pH of the solution about 12 using NaOH (0.5M), chitosan silver capped nanoparticles were precipitated and separated by centrifugation (12000 rpm in 30 min). After twice washing with deionized water, chitosan silver nanoparticles were dried at 40 °C and stored at dry chamber and room temperature for subsequent experiments.

2. 5. Procedure for Calibration Curves Chitosan capped silver nanoparticles (CS-AgNPs) Method: The equivalent of 100 µL at concentrations of 25-500 µmol mL^{-1} naproxen was transferred to a series of 5 mL bottles. In each bottle, 4.5 mL buffer solution (pH = 4) and 0.5 mL of CS -Ag nanoparticles at concentration of 0.5 $g.L^{-1}$ were added. The prepared standard was placed at room temperature (25 °C) for 8 minutes. The absorption of naproxen in a CS -Ag nanoparticles was measured by UV-vis spectrometer. To obtain the standard calibration curve, the absorption values versus the naproxen concentrations were plotted. Figure 2 illustrates absorption data were perfectly fitted for naproxen concentrations in the range of 25- 500 µmol mL^{-1}.

2. 6. Procedure for The Assay of Tablets Ten samples of 500 mg naproxen tablets from Tehran Daroo Company were used for the analysis of naproxen in tablets by using the proposed methods. The samples were well ground and turned into fine powder. The equivalent of 500 mg of naproxen powdered tablets, after careful weighing, was transferred to a 50 mL glass and dissolved in the 50mL amount of methanol, filtered through a Whatmann paper filter No. 41 and diluted in a 100 mL calibration flask with methanol to a specified volume.

3. RESULTS AND DISCUSSION

3. 1. Validation Parameters of Synthesis Chitosan -Capped Silver Nanoparticles Validation of chitosan-capped silver nanoparticles were characterized by ATM, DLS and ZP, FT-IR, and UV-Vis spectroscopy.

3. 2. UV-Vis Spectroscopy and Mechanism of Action In order to recognize enantiomers component, an interaction in three configuration dependent points are necessary based on researched. The structure of aromatic ring of naproxen and the intermolecular hydrogen bond between naproxen and chitosan-capped silver nanoparticles could possibly provide this "three-point" interaction. It was supposed that intermolecular hydrogen bond between naproxen and chitosan-capped silver nanoparticles and electrostatic interaction could possibly give this recognition. Therefore, this can be used in developing new reagents for determining via colorimetric assays [18]. In this way, the use of UV-vis spectroscopy is a very useful and reliable technique to confirm the initial properties of synthesized nanoparticles. In order to monitor the synthesis and stability of silver nanoparticles

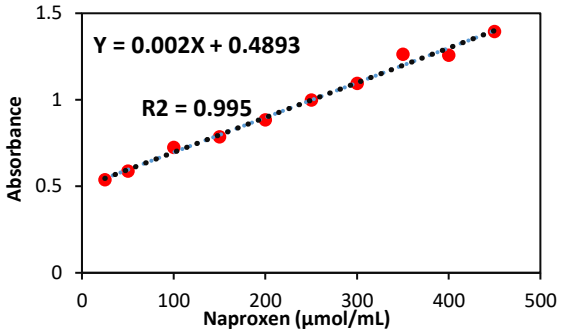

Figure 2. Calibration curve of naproxen with chitosan @Ag nanoparticles

[19] as well as the relationship between the plasmonic properties of silver nanoparticles and their morphology, a fast and easy UV -Vis spectroscopy method was developed for simultaneous monitoring the synthesis [24]. The synthesized chitosan capped silver nanoparticle solution was analyzed by UV-vis spectroscopy in the range of 270-620 nm. The UV-Visible spectrum for chitosan-capped silver nanoparticle is shown in Figure 3. The λmax of chitosan-capped silver nanoparticles was exactly observed at wavelength of 417 nm, which is the characteristic plasmon resonance band (SPR) of silver nanoparticles.

3. 3. FT-IR Spectra of Chitosan and Chitosan-Capped Silver Nanoparticles Figure 4 shows the FT-IR spectrum of standard chitosan and chitosan-capped silver nanoparticles. In the case of chitosan (Figure 4) as shown in this figure, the broad band marked at 3434 cm^{-1} is due to the overlap between the tensile vibrations O-H and N-H, both of them are semi-polysaccharides. In addition, the specified band in 2927 cm^{-1} is aliphatic which indicating of C-H bonds. Also, the tensile vibrations of the amide I, II and III bonds have caused the signals to appear at 1658 and 1600 cm^{-1} which is shown in Figure 4. However, silver ions were reduced to silver nanoparticles when liquid $NaBH_4$ added to $AgNO_3$ for the synthesized chitosan-capped silver nanoparticles. The FTIR spectrum of CS-Ag nanoparticles indicated that the nanoparticles exhibited absorption peaks at 3426, 1595, 1410, 656 cm^{-1} (Figure 4). The tensile bond pressures O - H and N - H in 3434 cm^{-1}originated from the primary hydroxyl and amino groups in chitosan were changed to 3426 cm^{-1}, which is indicating silver ions were chelated with both of amino and hydroxyl groups of chitosan [18]. The band at 1595 cm^{-1} corresponded to amide I due to carbonyl stretch in proteins. In addition, the peak at 1410 cm^{-1} refer to the C–N stretching in CS -Ag nanoparticles [9].

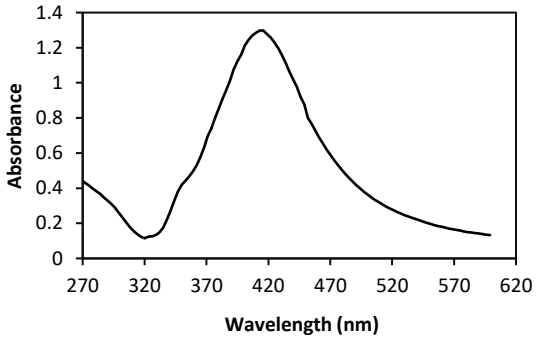

Figure 3. UV-Visible spectrum of chitosan @Ag nanoparticles

3. 4. Atomic Force Microscopy Surface morphology of chitosan capped silver nanoparticle was evaluated by AFM. AFM is provided an accurate information about the distribution of size and the shape of the particles [25]. Figure 5a shows the size distribution analysis of chitosan-coated silver nanoparticles by AFM which is in the range of 3–71.2 nm with an average size of 20±0.15.

It can be concluded that more than 50% of silver nanoparticle is in the range of 20 nm and indicating formation of nanoparticle in desirable size. The surface topography of chitosan capped silver nanoparticle and its properties in 2D and 3D picture are shown in Figure 5b. Also, the spherical shape of nanoparticles is clearly shown in these images which is proper and applicable.

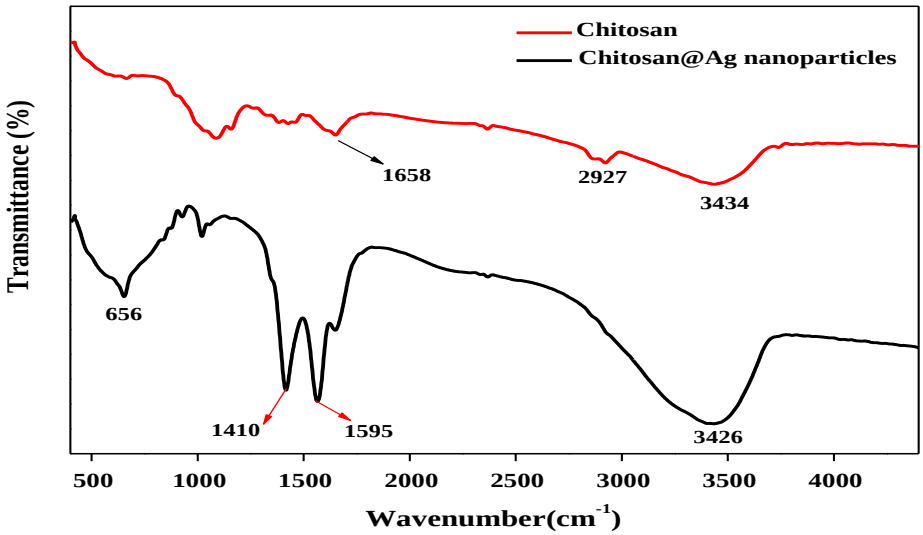

Figure 4. FT-IR spectra of chitosan (red curve) and chitosan @Ag nanoparticles (black curve)

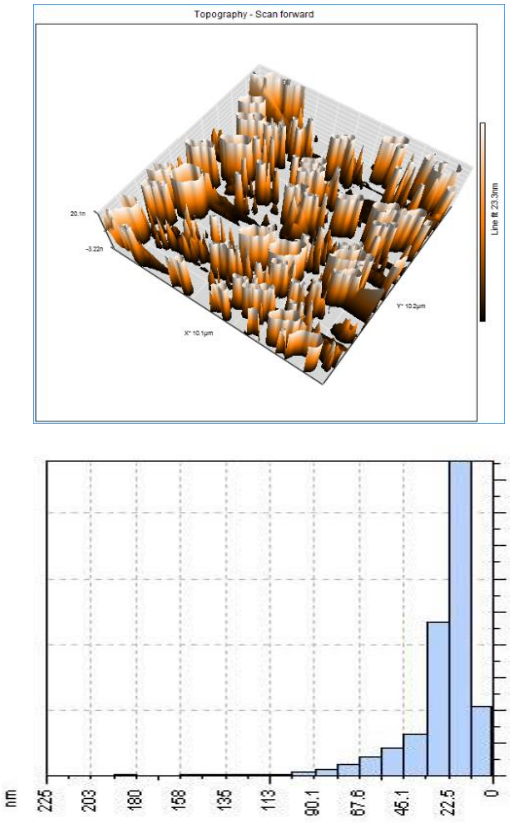

Figure 5. AFM results of chitosan @Ag nanoparticles: Surface topography (Left) and size distribiution (right)

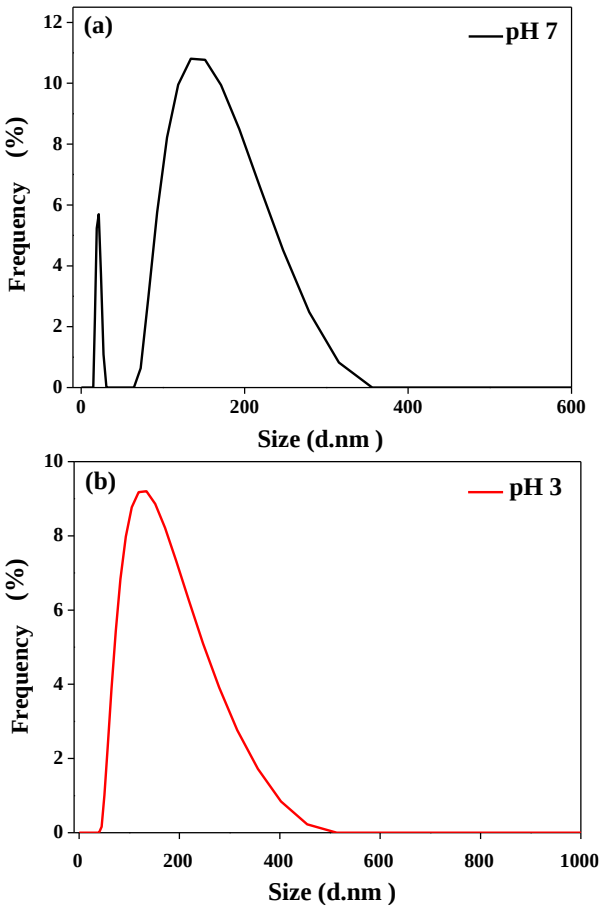

Figure 6. DLS spectra of chitosan @Ag nanoparticles at two pH values of (a) 7 and (b) 3

3. 5. DLS and Zeta Potential In order to investigate the scattering properties of nanoparticles and their hydrodynamic radius characteristics, DLS and zeta potential analysis have been used [19]. Size distribution and poly-dispersity index (PDI) are the two most important factors in the DLS test which are dependent on physio-chemical properties of nanoparticle in solvent. These experiments were carried out at two different pH to examined its effectiveness on nanoparticle size distribution and its poly-dispersity. It can be mentioned that size distribution lower than 150 nm is acceptable as nanoparticle. In addition, based on literature, PDI value in the range of 0.1 to 0.4 is appropriate as poly-dispersed and stable solution [19]. However, Figures 6a and 6b represented the results of DLS analysis for chitosan capped silver (CS-Ag) nanoparticles at pH of 7 and 3, respectively. Because of chitosan insolubility at neutral pH, nanoparticle size was increased (448 nm) and its DPI was 0.618 which is not acceptable.

These results indicate that CS –Ag nanoparticle reagent has resulted in agglomeration at neutral pH, so it can cause limitation of the reagent applications. However, the obtained result at pH 3 showed that the mean diameter of CS- Ag nanoparticles was 116.5 nm and PDI was 0.385, which is less than 0.4. These finding indicated that a homogeneous dispersion of the CS-Ag nanoparticles produced at acidic pH. It can be noted that chitosan polysaccharide is completely soluble at acidic pH. Based on literature, these results can improve nanoparticle size distribution and PDI. In addition, the zeta potential test was used to measure the electrostatic potential at the electrical double layer surrounding a nanoparticle in the solution. Based on literature, nanoparticles with a zeta potential between -10 and +10 mV were categorized in the region of neutral, while nanoparticles having zeta potentials of greater than +30 mV or less than -30 mV were indicated strongly cationic and strongly anionic strengths, respectively. On the other hand, high zeta potential (greater than ±30 mV) of nanoparticles demonstrated that its great stability or its strong resistance against the aggregation, flocculation, and coagulation. Several factors are affected the zeta potential of CS-Ag nanoparticles, for instance particle size and structure, ionic strength, pH of the solution, etc. Therefore, zeta potential of CS-Ag nanoparticles was measured at pH 7 and 3 (see Figures 7). As can be seen,

the zeta potential is approximately neutral (14.4 mV) at pH 7 while it is strong anionic (-24.8mV) at pH 3 which is refer to chitosan surface charge and its functional groups. Therefore, the new proposed reagent exhibited excellent stability at acidic pH at room temperature.

3. 6. Naproxen Determination and Validation Method

3. 6. 1. linearity of the Calibration The first step in the method development is the linearity of the calibration function. The correlation of coefficient is often used as a factor that shows the linearity of the calibration curve. The calibration curve for naproxen absorption with CS-Ag nanoparticles was linear in the concentration range of 25 to 500 µmol mL^{-1} with a correlation coefficient of 0.995. (see Figure 2). The linear equation obtained by least squares regression method were y= 0.4893+0.002X that y is the absorption intensity (in arbitrary units) and x is the concentration of naproxen in (µmol mL^{-1}) which constant obtained values and R square correlation coefficient are equal to B = 0.002, A = 0.4893 and R^2 = 0.995, respectively. It can be concluded that the proposed reagent and analysis method had been correctly functioned.

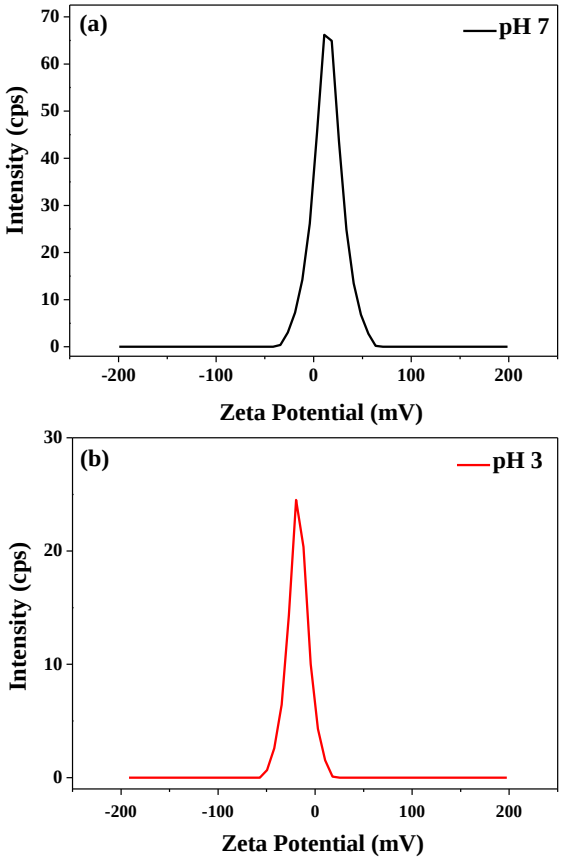

Figure 7. Zeta potential of chitosan @ Ag nanoparticles at two pH values of (a) 7 and (b) 3

3. 6. 2. Absorption Spectrophotometric As shown in Figure 8, the absorption spectra of naproxen and the complex of naproxen and chitosan-capped silver nanoparticles were measured in the range of 230-630 nm. Naproxen at concentration of 50 µL (0.001 M) in methanol showed two absorption peaks which were observed at 262 and 273 nm. The effect of reaction time and pH of the complex of chitosan capped silver nanoparticles and naproxen for finding optimum conditions with maximum stability and sensitivity in absorption was investigated.

3. 7. Optimal Conditions for Detection of Naproxen with Chitosan Silver Nanoparticles

3. 7. 1. Effect of Reaction Time To finding a reagent with minimum reaction time is essential parameter in clinical laboratory. So, this is important for developing a new reagent that reaction between them reach to stable condition in minimum time and stay constant after passing time. Therefore, the effect of the reaction time between chitosan capped silver nanoparticles (reagents) and naproxen on naproxen adsorption was investigated at different time intervals. Initially, the absorption decreased and gradually peaked over time after 8 minutes, then reached to a steady state value after 10 minutes and remained stable (see Figure 9). It can be concluded that the optimum reaction time of 8 min was defined. The reaction time of 8 min was used in the subsequence experiments. This short reaction time is a positive point for a new reagent which reach to stable condition.

3. 7. 2. Effect of pH Chitosan is a cationic polyelectrolyte biopolymer which can be dissolved in acidic pH. The reason is most probably caused by amine groups on chitosan main chain. Therefore, it is soluble in aqueous phase at acidic condition where amine groups

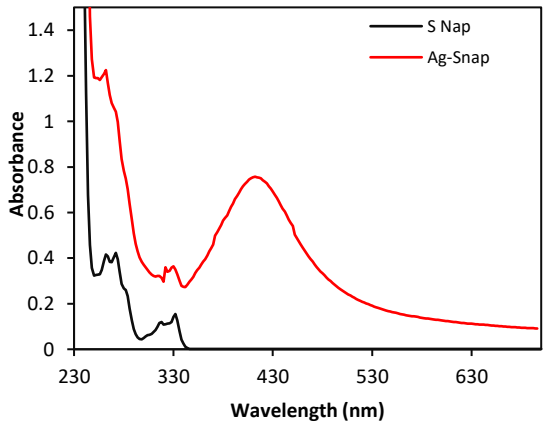

Figure 8. UV-Vis spectrum of pure naproxen and complex of naproxen with chitosan @Ag nanoparticle

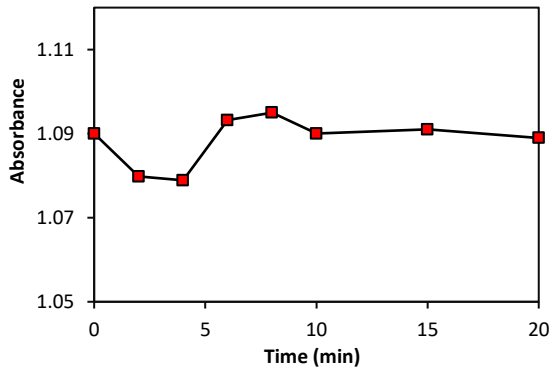

Figure 9. Effect of reaction time on the formation of naproxen- nanoparticles complex

are positively charged. However, chitosan at pK value of 6.5 possess neutral charges. Because of chitosan changeability in various pH, determining appropriate pH is critical matter for silver nanoparticle which capped via chitosan [26, 27]. In addition, based on our experiments chitosan silver nanoparticles are not stable at pH <3.0 and pH> 8.0 [18]. Therefore, the effect of pH in the solution on the stability of chitosan silver nanoparticles (reagent) and naproxen absorption was studied in the range of 3-6. As can be seen the spectrophotometric spectra of samples in Figures 10a and 10b, the maximum intensity of naproxen absorption was observed at pH = 4.0; consequently, the optimum pH for the rest of experiments was chosen to be 4.

3. 7. 3. Determination of Naproxen The existing solution was diluted using methanol at appropriate concentrations in the working range. Then the amount of naproxen in the tablets were measured using the proposed method and the new reagent CS -Ag nanoparticles (see Table 1). The reliability of the amount of naproxen calculated based on the standard calibration curve and reported in Table 1. For examination of the proposed reagent accuracy, different concentration of tablets with 20 μgmL^{-1} variations were prepared and analyzed by the mentioned method. The achieved results and the amount of recovery values are summarized in Table 2, respectively.

3. 7. 4. Detection Limits (LOD) and Quantitative Limit (LOQ) The Limit of detection (LOD) and quantification (LOQ) are the two most important characteristics in validation of a new method. The lowest concentration of analyte in a sample which can be determined with the acceptable accuracy in the defined test conditions is called the detection limit (LOD) [28]. Normally a reagent is not able to exact measure the analyte concentration; although, this claim may have declared in the reagent package. In order to distinguish

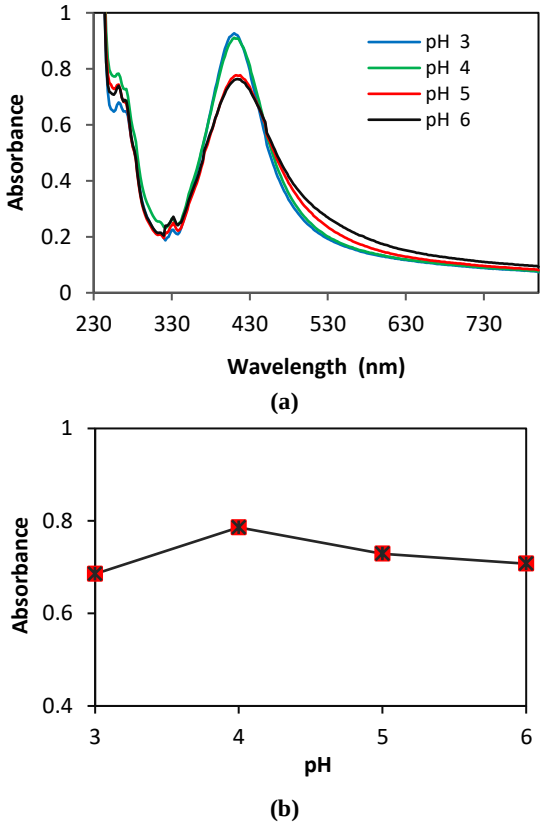

Figure 10. UV-Vis spectrum (a) and absorbance of naproxen at variuos pH values

between the analytical signal and the analytical noise in the absence of analyte, there must be a sufficient concentration of analyte [28]. So, the lowest level of analyte concentration which produced a detectable response is called the detection limit, which is usually three times the noise level. Therefore:

$$LOD = 3\sigma_A/B \quad (1)$$

where the σ_A standard deviation from the fitted regression line is calculated and the B is slope of calibration curve. Standard deviation of the y-intercept of the regression line Sy/x, i.e. standard error of estimate. In the latter method, only the error in the intercept is considered. A better alternative is the equation proposed by Winefordner and Long expressed as follows [2]:

$$LOD = k\,[\sigma^2_{b1} + \sigma^2_A + (A/B)^2\,\sigma^2_B\,]^{1/2} \quad (2)$$

TABLE 1. Determination of naproxen in tablet dosage form using proposed method

Method	Naproxen labeled amount (mg)	Found (mg)	Recovery (%)
chitosan -capped silver nanoparticles	500	503.44	100.688

TABLE 2. Determination of naproxen in tablet dosage form using the standard addition technique

Sample	Taken (µg mL^{-1})	Added (µg mL^{-1})	Found (µg mL^{-1})	Recovery (%)
Naproxen 500 (mg)	100	0	99.67	99.670
		20	119.43	99.525
		40	137.95	99.535
		60	159.56	99.725

TABLE 3. Comparison of the developed method with reported methods

Method	Linearity Coefficient	Relative Error	Ref.
HPLC	0.999	-	[30]
Capillary electrophoresis	0.9969	5	[25]
Spectroscopy	0.9988	3.5	[31]
Spectroscopy	0.999	1.4	[18]
Spectroscopy	0.995	1	This method

Where k is a constant value, which is usually equal to 3, also b_l is the standard deviation of a set of iterations from the empty sample solutions, σ^2_B is the standard deviation of the slope, σ^2_A standard deviation from the fitted regression, the B and A are slope and coefficient of calibration curve respectively. The limit equations (LOD) and quantitative limit (LOQ) according to the International Council for Harmonisation of Technical Requirements for Human Pharmaceuticals Use (ICH) given as follows [29]:

$$LOQ=3.3\sigma/s \quad (3)$$

$$LOQ=10\sigma/s \quad (4)$$

Where the σ standard deviation from the fitted regression line is calculated and the S is slope of calibration curve. In this work, the detection limits (LOD) and quantitative limit (LOQ) for the proposed method based on Equations 3 and 4 were calculated 0.022 $mol.L^{-1}$ and 0.066 $mol.L^{-1}$, respectively. It can be noted that the obtained results of LOD and LOQ are in defined range and so acceptable.

3. 8. Validation Method The characteristics of synthesized chitosan capped silver nanoparticles (reagent) were determined by ultraviolet spectroscopy (UV), Fourier transform infrared spectroscopy (FT-IR). The results were completely in line with the data reported by Tashkhourian et al. [18] and Jafari et al. [9]. In addition, its morphology and size distribution were confirmed by atomic force microscopy (AFM), dynamic light scattering (DLS) and zeta potential (ZP) analyses in optimal conditions. It can be concluded that the proposed reagent is stable in acidic condition which is proper for determination of naproxen. In order to confirm the validity of the new developed method, limits of detection (LOD) and quantitation (LOQ), reproducibility, reproducibility and its accuracy were examined according to ICH guideline. Also, linearity of applied method was investigated in the concentration of 25-500 $\mu mol.mL^{-1}$ naproxen, and correlation coefficients of 0.995 was achieved. In addition, a computational method was developed to define the limits of detection (LOD) and quantitation (LOQ) which calculated 0.022 and 0.066 $mol.L^{-1}$, respectively. The performance of the proposed method was compared with the merit of the developed method with reported methods in literature (see Table 3). {Absalan, 2012 #46}

4. CONCLUSION

This research has demonstrated that chitosan capped silver nanoparticles are a suitable probe for the detection of naproxen using Uv-vis spectrophotometry. Based on the results, the accuracy of this method was very good for determining the amount of naproxen in tablets. Analysis of statistical data, the reproducibility and accuracy of this method demonstrated that the use of this novel method is valuable and practical for determination of naproxen in pharmaceutical formulations. The linear dynamic range and precision, accuracy of developed method chitosan capped silver *nanoparticles* indicate that the figures of merit were comparable with most reported methods for the determination of naproxen. The spectrophotometric method using chitosan capped silver nanoparticles was quite suitable and applicable for the detection of naproxen in bulk and drug formulation.

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Persian Abstract

چکیده

ناپروکسن یک داروی ضد التهاب غیراستروئیدی است که بطور گسترده برای درمان حاد تا مزمن استفاده میشود هدف از این کار توسعه یک روش اسپکتروفتومتری ساده وجدید برای تشخیص ناپروکسن در فرمولاسیون دارویی است که برای اولین بار توسط نانو ذرات نقره با پوشش کیتوسان ایجاد شد ساختار و مرفولوژی نانو ذرات باطیف سنجی مرئی –فرابنفش,(UV-VIS) تکنیک, FTIR میکروسکوپ اتمی, (ATM) تکنیک DSL وآنالیز زتاپتانسیل (ZP) تحت شرایط بهینه تعیین شد نتایج نشان داد که ، نانوذرات نقره پوشانده شده با کیتوزان تقریباً با اندازه ذرات ۱۰۰ نانومتر وشاخص پراکندگی385/0 (PDI)و پتانسیل زتا آنیونی قوی (۲٤/۸–میلی ولت) در شرایط اسیدی بودند. مشخص شد که کیتوزان به عنوان یک انتخاب کایرال قادر به تشخیص ناپروکسن در شرایط بهینه آزمایش است. این روش برای تعیین ناپروکسن در فرمولاسیون قرص های دارویی موفقیت آمیز بود. انحراف استاندارد نسبی ۱.۰٪ برای تجزیه و تحلیل ناپروکسن در نمونه های واقعی تعیین شد. اعتبار سنجی این روش ، از جمله حد تشخیص و حد کمی با توجه به دستورالعمل های ICH به طور دقیق تأیید شد. بر اساس این روش ، حد تشخیص((LOD) و حد کمی(LOQ) ناپروکسن به ترتیب ۰۲۲ / و۰٦٦/ میلی مول بر لیترمحاسبه شد. تجزیه و تحلیل داده های آماری ، قابلیت تکرار و دقت این روش نشان داد که استفاده از این روش جدید برای تعیین ناپروکسن در فرمولاسیون های دارویی ارزشمند و عملی است.