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Design and Evaluation an *Origanum majorana*-Capped AgNPs Sensor: Determination of Trace Megestrol Drug in Urine and Blood Samples using Kinetic Spectrophotometric Method

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Abstract

Megestrol drug is a synthetic steroid progesterone, and it is used as an anti-plasma agent to treat advanced breast cancer or endometriosis. In this study, for determination of megestrol drug in solution using kinetic spectrophotometric method, we prepared a solution of Origanum majorana-capped AgNPs utilizing sodium borohydride as a stabilizer sensor. The calibration curve was linear in the range of (0.01 to 10.0 μg L^{-1}). The standard deviation of (1.8%), and detection limit of the method (0.023 μg L^{-1} in time 8 min, 345 nm) were obtained for Sensor level response *Origanum majorana*-capped AgNPs with (95%) confidence evaluated. The observed outcomes confirmed the suitability recovery and a very low detection limit for measuring the megestrol drug. The method introduced to measure megestrol drug in real samples such as urine and blood was used and can be used for other drugs and hospital samples.

Keywords: Megestrol Drug, *Origanum majorana*-capped AgNPs, Sensor, Measurement, Kinetic.

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Introduction

Determining the amount of drug used in the biological sample is very important to follow the amount of its effect in the body system. Accordingly, different methods with high sensitivity, selectivity and efficiency, as well appropriate analysis for the determination, extraction and measurement are presented of drugs in real samples [1]. One of the biggest problems in the decomposition of biological samples is the existence of different species and their effect on the decomposition process of the drug. For this reason, many drug measurement methods are based on separation methods such as gas chromatography and high-performance liquid chromatography that are very time-consuming methods with difficult working conditions [2,3]. Megestrol acetate, 17-(acetyloxy) -6-methyl-progen-4,6-din-3,20-dione show in (Figure 1), a synthetic steroid progesterone, is widely used to treat loss of appetite and weight loss in AIDS patients. Also, it is used as an anti-plasma agent to treat advanced breast cancer or endometriosis. Therefore, knowing the necessary care while following patients is of special importance [4,5]. Nowadays, surgery, chemotherapy and radiotherapy are known as the best way to treat breast cancer, but they all lead to hypoxia to varying degrees. It is necessary to target anti-cancer drugs so that they only affect cancer cells and also to use the minimum concentration of drugs so that the toxic effects of the drug on normal cells are reduced [6,7]. In that respect, for tracing one medicament in pharmaceutical and biological samples, Lately, for discerning and accurate reorganization of species (1-inorganic 2-organic and 3- biomolecules) in different intricate matrices, and determining environmental pollution caused by drugs in the ecosystem and biological samples attention has been using of spectrometric method and by sensors metal nanoparticles sensor [8,9].

Due to the profitable application of metal nanoparticles, technologies have taken advantage of nanoscale materials in a variety of fields from chemistry to medicine [10,11]. The forms, sizes, and structures of metallic nanomaterials which are extensively linked to their chemical, physical, and optical characteristics, set the ground for successful use of them in technologies. In this respect, the exceptional physical, chemical, and biological properties of silver nanoparticles (AgNPs) have been confirmed. This exceptionality arises from the size, form, composition, crystallinity, and structure of AgNPs in comparison with its bulk form [12]. AgNPs can by various methods such as the application of stabilizing and reducing chemicals of hydrate and sodium borohydride, formaldehyde, polyethylene glycol, glucose, electrochemical heating, photochemical reduction prepared [13]. Therefore, measures have been taken to investigate their exclusive properties and employ them in practical applications like anti-bacterial and anti-cancer therapeutics [14], diagnostics and optoelectronics [15], water disinfection [16], and other clinical/pharmaceutical applications [17]. Furthermore, AgNPs has been widely used in antimicrobial applications due to its

antimicrobial properties. The exclusive properties of AgNPs have application in the fields of biosensing, nanomedicine, pharmacy, biomedical, detergents and determining environmental pollution caused by drugs in the ecosystem and biological samples equipment [18].

This study aimed to find a simple, fast and very sensitive method for identifying and measuring the drug megestrol by *Origanum majorana*-capped AgNPs biosensor. With an initial isolation method to measure this drug, various effective factors such as pH, drug megestrol concentration, biosensor concentration, time Reaction, ionic strength, etc., on the response of the method and obtaining the optimal test values and the linear range, detection and accuracy of the method were presented in the measurement of megestrol drug. Also, the performance of the method with routine clinical techniques, the accuracy of the method, identification and measurement of megestrol drug by a kinetic Spectrophotometric new method in real samples (blood serum) was checked. The chemical *Origanum majorana*-capped AgNPs sensor made it possible as an excellent sensor with reproducibility, good recovery and a very low detection limit for measuring megestrol drug. The method by kinetic Spectrophotometric introduced to measure megestrol drug in real samples such as urine and blood was used and can be used for hospital samples.

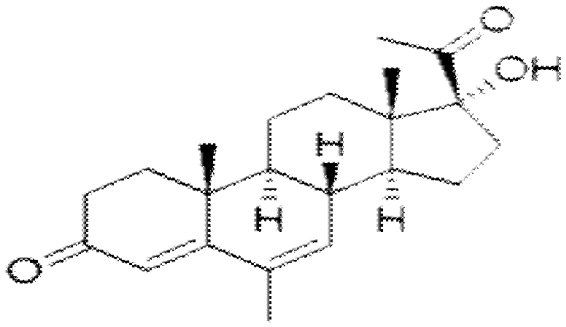

Figure 1. The Structures of Megestrol Drug.

Experimental

Reagents and materials

All chemicals including Silver nitrate ($AgNO_3$) and Sodium borohydride ($NaBH_4$) were provided by Merck Company. Megestrol medication (98.0%) was purchased from (Cipla, Indian Company). for pH < 7.0, as buffer solutions were prepared from 1 ml of boric acid/acetic acid/phosphoric acid (1.0 M), and for pH >7.0 was adjusted by the addition of 0.2M sodium hydroxide, DD H_2O (Double distilled water) was used in the preparation of the solutions.

Instruments

UV–visible spectra, drugs concentrations were determined and their measurements were done using a Maya Pro 180 spectrophotometer (Shimadzu Company, Japan). The registration of FT-IR or Fourier transform infrared spectra were done on a PerkinElmer (FT-IR spectrum BX, Germany). SEM (Scanning electron microscopy: KYKY-EM 3200, Hitachi Firm, China) under an acceleration voltage of 26kV) was used to study the morphology of samples. TEM images (Transmission electron microscopy) were taken on a (TEM, JEOL, Hitachi Company, China). For the measurement of pH, the pH/Ion meter (model-728, Metrohm Firm, Switzerland, Swiss) was employed.

Pretreatment of real samples

Urine samples

In a 50 mL beaker, treatment of a 10 mL portion of a urine sample (or a spiked urine sample) in hospital (Ahvaz, Shiraz, and Boushehr) were done using 10 mL of concentrated HNO_3 (63%) and an $HClO_4$ (70%) mixture of 2:1 and then covered with a watch glass. Then on a hot plate, the treated sample of the balloon was heated (100°C 15 min/ 150°C 10 min). Next by removing the watch glass, the acid was left to evaporate to dryness at 150°C. After that by adding $HClO_4$ (3 mL) to the resulting white residue, the mixture was heated at 160°C to dryness. The whole heating process was done under a hood while necessary safety precautions were practiced. Upon adding five milliliters of 1 M H_2SO_4, the mixture was heated at 150°C for 1 min and then with the help of a 50 mL volumetric flask, the desired volume was made up to the mark. Seven mL of the obtained clear solution was picked and the analysis was performed according to the explained procedure [19].

Blood sample

In the presence of an oxidizing agent and 10 mL of concentrated HNO_3, the exact amount of homogenized human blood sample (20 mL) in hospital (Ahvaz, Shiraz and Boushehr) were digested in a 200 mL balloon and then 2 mL $HClO_4$ 70 % was added and heated for 1 h. With the help of a Whatman No. 42 filter paper into a 250 mL calibrated flask and its pH was adjusted to the desired value and diluted to mark with de-ionized water. In all of real and synthetic sample amount of megestrol drug was found by standard addition method [20].

Synthesis of Origanum majorana-capped Ag NPs

In this regard, the following details of the materials are important to consider in their synthesis: surface property, size distribution, apparent morphology, particle composition,

dissolution rate. *Origanum majorana*- Capped Ag NPs were prepared by the reduction of $AgNO_3$ with $NaBH_4$ as a modifier according to the method in the literature [20]. Briefly, 10.0 mL of *Origanum majorana* (2.0 mM) solution was added into the reaction flask that contained 90.0 mL of $AgNO_3$ (2.0 mM) solution under vigorous stirring. After 15 min, 1 mL of $NaBH_4$ (2.0 mM) added into the above solution at room temperature and stirred for 1 h. UV–visible spectrum of *Origanum majorana*- capped AgNPs. The inset picture show *Origanum majorana*- capped AgNPs. The dark colloidal solution color was changed to bright yellow, confirming that the formation of *Origanum majorana*- capped AgNPs. The *Origanum majorana*- capped AgNPs solution was stored in the dark at $4.0 \pm 2.0^{\circ}C$ to remain stable for several weeks (Figure 2).

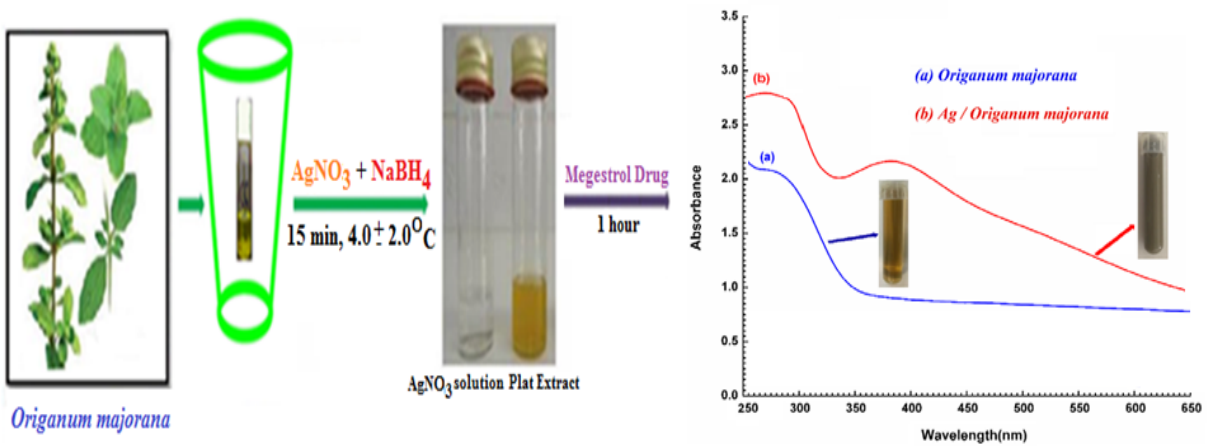

Figure. 2. Synthesis of *Origanum majorana*-capped AgNPs.

Procedure kinetic Spectrophotometric Detection measurements

The ensuing steps have been considered for a kinetic Spectrophotometric method experiment in the current study, at the initial step: Some of the sample solution containing 1 ml of megestrol drug (10.0 µg L^{-1}) was added to a 10 ml volumetric balloon. Then 1 ml of utilizing sodium borohydride as a stabilizer for sensor (2.0×10^{-2} mol L^{-1}) was added to the flask. Now, by increasing the first drop of 1 ml of *Origanum majorana*-capped AgNPs solution (2.0×10^{-2} molL^{-1}) into a balloon, the reaction start time is recorded by a timer, after 5 seconds from the start of the reaction the solution is stirred for 30 seconds, Subsequently, an adequate amount of the solution was added to a 1 cm cell. Finally through using of UV–visible spectrum (AAb), the measurement of the difference between the quantities of the absorption in wavelength equal to (345 nm) in a time interval (1.0 -8.0 min) was carried out. By adding megestrol medicament to the solution, it was observed that absorbance kinetic Spectrophotometric of the *Origanum majorana*-capped AgNPs at the wavelength of (345 nm) dropped. At the same time, with the help of spectrophotometry and UV–

visible spectrum (AAb), the apparent spectral evolution including the formation of a well-defined isosbestic point at around (345 nm) was estimated. All reaction steps were repeated by increasing the concentration (0.2 μgL^{-1}) of the megestrol drug every 30 seconds. Moreover, the mentioned steps were repeated for a reaction in the absence of megestrol medicament (Abs b). Eventually, (Abs a) Abs blank – Abs sample was calculated. The reaction of the megestrol drug by *Origanum majorana*-capped AgNPs was detected in the acidic medium in its wavelength (345 nm, Fig. 3A and Fig. 3B), demonstrate the absorption spectra in an aqueous solution [22,23].

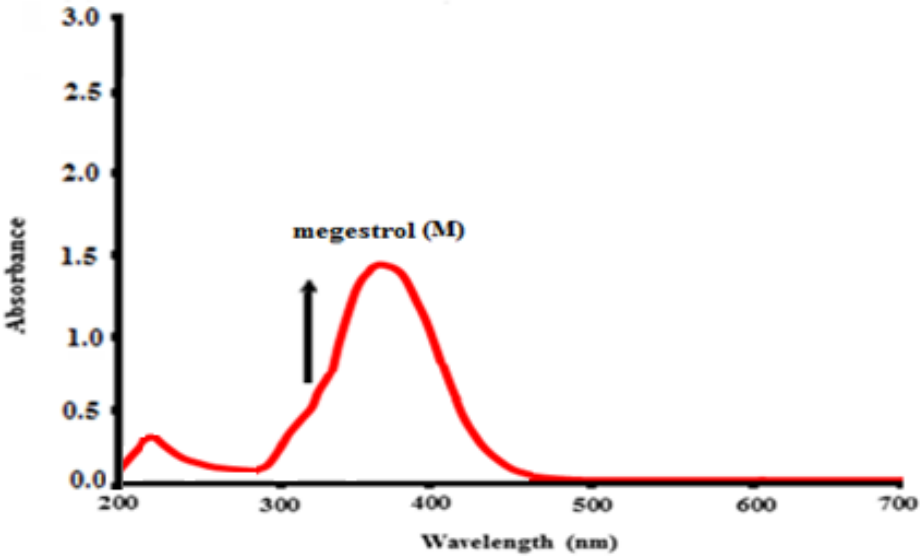

Figure 3A. The absorption megestrol drug.

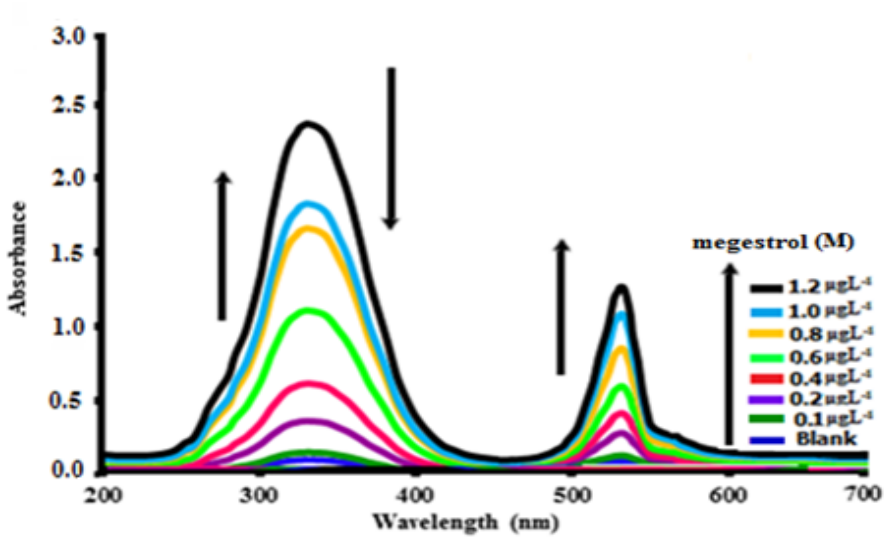

Figure 3B. The absorption *Origanum majorana*-capped AgNPs and megestrol medicament 30 sec, and increasing concentration of megestrol drug solution (0.2µg L^{-1}).

Results and discussion

Characterization of sorbent

Figure 4, clearly shows the FTIR spectrum of *Origanum majorana*-capped AgNPs loaded on activated carbon. The wide signals at ≤900 and 1048 in Ag – O, 1386-1422 cm^{-1} are ascribable to C–H stretching from *Origanum majorana*-capped AgNPs, and the ones at 1634cm^{-1} to C=O bonds. The appeared signal at 2027 cm^{-1} is relative to C–H stretching while the one at 3412 cm^{-1} is attributed to – OH stretching[24]. EDX (energy-dispersive X-ray spectroscopy) spectrum of (fig.5a) The EDX transmittance spectrum of the prepared *Origanum majorana* and (fig.5b) EDX spectrum recorded from a film, after the formation of silver nanoparticles [25]. Different X-ray emission peaks are *Oiganum majorana*-capped silver nanoparticles. The adsorption of megestrol drug and based on Fig.5a, which is the XRD pattern of the *Origanum majorana*-capped AgNPs, the signals at 38.07 (111), 44.26 (200), 64.43 (220), and 77.35 (311) are ascribable to diffractions and reflections from the carbon atoms[26]. The perfect crystalline nature of the material was proven after functionalizing with *Origanum majorana*-capped AgNPs however the great intensity of the signal at 38.07 (111) confirmed that there has been a slight amount of material in an amorphous state. The perfect synthesis of *Origanum majorana*-capped AgNPs is obvious through looking at the XRD pattern. In Fig.6a, and Fig.6b, the image TEM of the prepared *Origanum majorana*-capped AgNPs. The morphological properties of the samples scrutinized by SEM are exhibited. By looking at (Fig.7), the smoothness, homogeneity, and tidiness of *Origanum majorana*-capped AgNPs are confirmed. Even uniformity size distribution is observable in (Fig.7). After surface modification, the *Origanum majorana*-capped AgNPs became uneven, larger, and bundled [26].

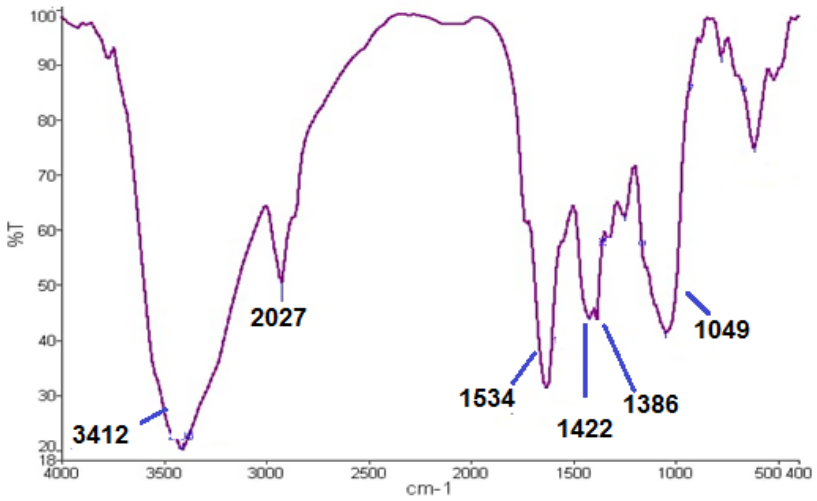

Figure 4. FT-IR transmittance spectrum of the prepared *Origanum majorana*-capped AgNPs.

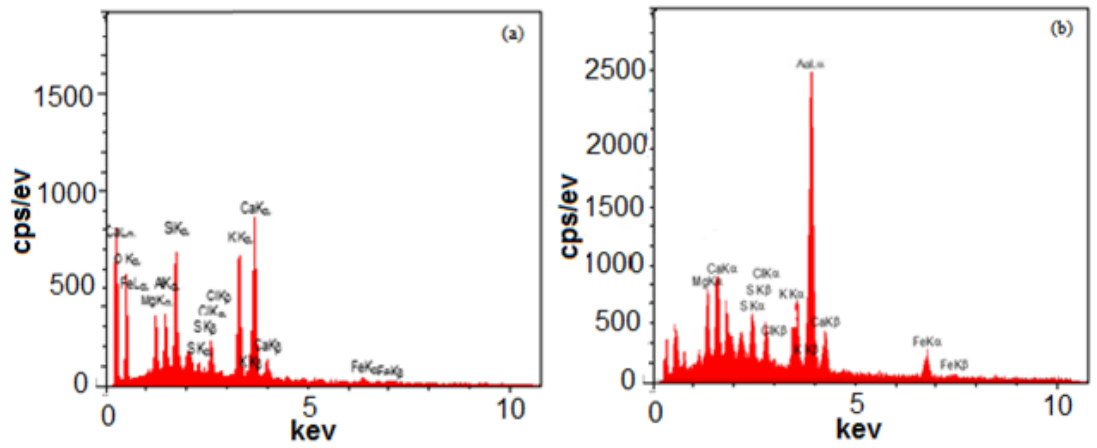

Figure 5. (a) The EDX transmittance spectrum of the prepared *Origanum majorana* and (b) EDX spectrum recorded after formation *Origanum majorana*-capped silver nanoparticles.

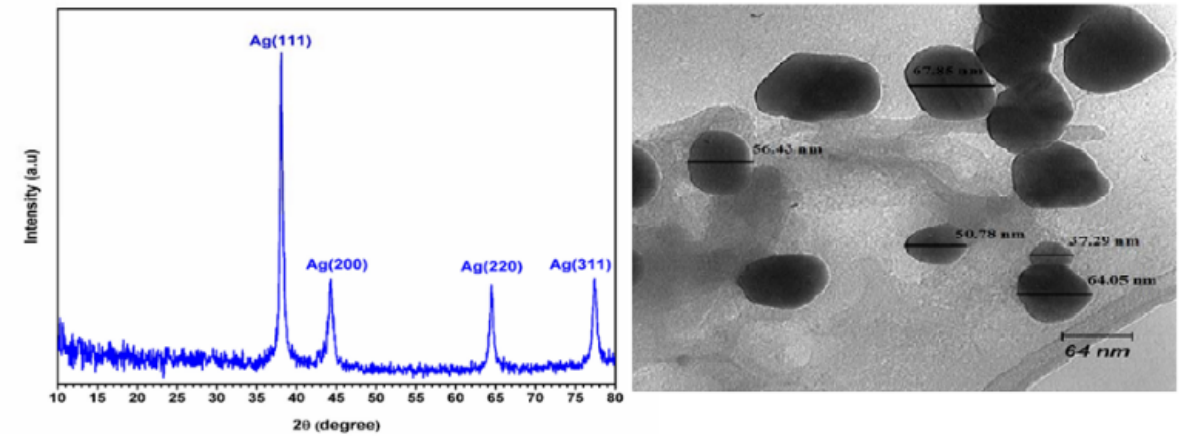

Figure 6. The (a) XRD image and (b) TEM of the prepared *Origanum majorana*-capped AgNPs.

Optimization of decomposition

It would be interesting to know that in the presence of megestrol drug, there observed a considerable improvement in the effectual colorimetric sensing and absorbance kinetic Spectrophotometric method of the as-prepared *Origanum majorana*-capped AgNPs sensor. Obtaining an exceptionally sensitive response in detecting megestrol drug rests upon the systematic optimization of pH values, *Origanum majorana*-capped AgNPs sensor and incubation time. In this section, the best type of buffer and its volume for maximum absorption megestrol drug with *Origanum majorana*-capped AgNPs sensor are investigated. At this step, the procedure is as follows:

In 10 ml balloons, 1 ml of megestrol drug (10.0 μg L^{-1}) and a volume of each type of acetic acid/boric acid/phosphoric acid were buffered. Then 1 ml of 1 *Origanum majorana*-capped AgNPs sensor (2.0×10^{-2} mol L^{-1}), 1 ml of utilizing sodium borohydride as a stabilizer for sensor (2.0×10^{-3} mol L^{-1}), to the solution were added inside the balloon and after 8 minutes, the adsorption of the

solution was read by UV–Visible spectrophotometry. Based on the results, 1 ml of acetic acid buffer shows the highest percentage for the determination of megestrol drug, so acetic acid /tri chloric acetate buffer (1.0 M) to adjust the pH solution as the optimal buffer.

The great impact of the pH value of the reaction solution on the interaction between *Origanum majorana*-capped AgNPs and megestrol drug was undeniable. To examine the influence of *Origanum majorana*-capped AgNPs on the reaction rate, 1ml megestrol drug (10.0 μgL^{-1}) solution, *Origanum majorana*-capped AgNPs sensor (2.0×10^{-2} mol L^{-1}), and 1 ml sodium borohydride (2.0×10^{-3} $molL^{-1}$) were mixed in the 10 ml volumetric flask using DD H_2O (Double distilled water). After measuring the absorbance intensity of the solution, a thorough investigation was carried out on the absorbance pH values in the range of (1-8) for the megestrol drug- *Origanum majorana*-capped AgNPs complex at (345 nm).

As evident in Fig. 7 A, absorbance kinetic Spectrophotometric rapidly on changing the pH from 1.0 to 5.0, while it decreased at pH values higher than 5.0. This phenomenon might be because of the weak complexion at lower pH values (pH <5.0). On the other hand, the reduced response of the proposed *Origanum majorana*-capped AgNPs sensor for the determining megestrol drug at pH > 5.0 could be due to a possible formation of the hydroxide of megestrol drug in solution. Thus, pH 5.0 was selected as a favorable pH for all subsequent experiments. Concurrently, 1 ml megestrol drug (10.0 μg L^{-1}) solution, 1 ml sodium borohydride (2.0×10^{-3} $molL^{-1}$) and 1ml *Origanum majorana*-capped AgNPs (0.5×10^{-3} to 4.0×10^{-2} $molL^{-1}$), were mixed in a volumetric flask 10 ml using DD H_2O (Double distilled water) to find out about the impact of *Origanum majorana*-capped AgNPs sensor on the reaction rate. Again absorbance intensity of solution was assessed. The previously mentioned operation has been replicated for blank solution (the solution in the absence of megestrol drug). The findings are exhibited in Fig. 7B. Consequently (2.0×10^{-2} $molL^{-1}$) based on those findings was determined as the perfect concentration [27, 28].

To look over the efficacy of sodium borohydride concentration, with a help of volumetric flask 10 ml, firstly 1 ml megestrol drug (10.0 μg L^{-1}) solution, 1 ml sodium borohydride with different concentration (0.05 to 3.0×10^{-3}mol L^{-1}), and 1 ml *Origanum majorana*-capped AgNPs, (2.0×10^{-2}mol L^{-1}), the estimation for sorption of solution was carried out after 8.0 min. The aforementioned steps were repeated in the absence of megestrol drug (blank solution). The findings are exhibited in Fig. 7 C. The decision on desired concentration for sodium borohydride at based on the results was made to be (2.0×10^{-3}mol L^{-1}). Also, the impact of reaction time on the absorbance spectrum was investigated. Based on (Fig. 7 D), it has become apparent that the absorbance intensity enhanced expeditiously and reached its peak at around 8 min. After 8 min, a relative stability was spotted in

the absorbance intensity. Thus, 8 min was determined as the perfect reaction time in this experiment [28].

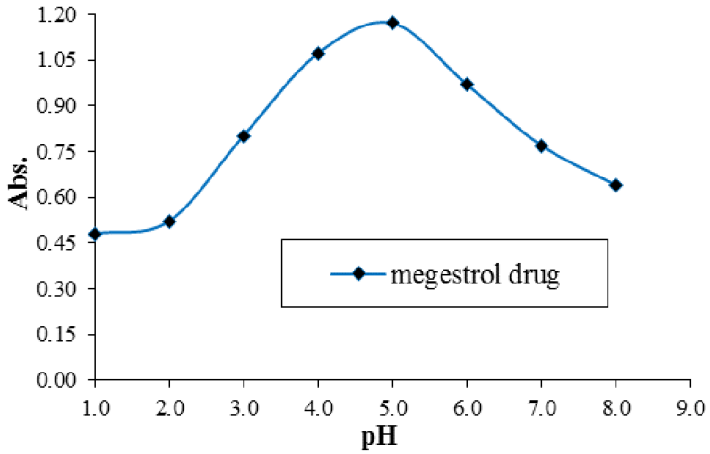

Figure 7A. The impact of pH in the absorbance rate. (aqueous sample volume, 10 mL: *Origanum majorana*-capped AgNPs, 2.0×10^{-2} M, sodium borohydride, 2.0×10^{-3} M, megestrol = 10.0 μgL^{-1}, time 8 min, 345 nm).

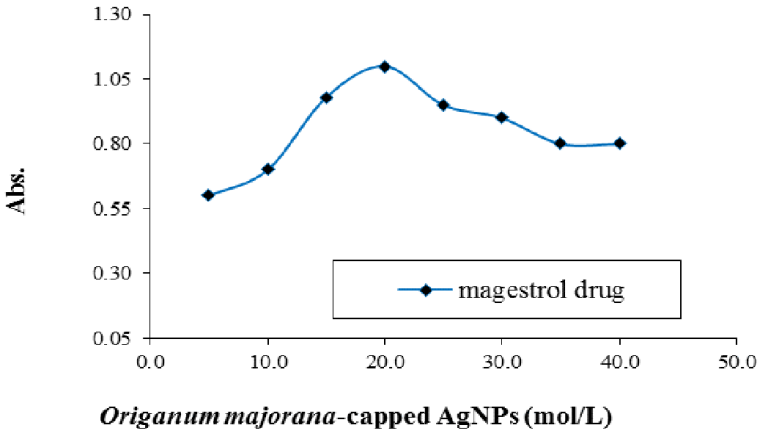

Figure 7B. The impact of *Origanum majorana*-capped AgNPs in the absorbance rate. (aqueous sample volume, 10 mL: sodium borohydride, 2.0×10^{-3} M, pH =5, megestrol drug = 10.0 μgL^{-1}, time 8 min, 345 nm).

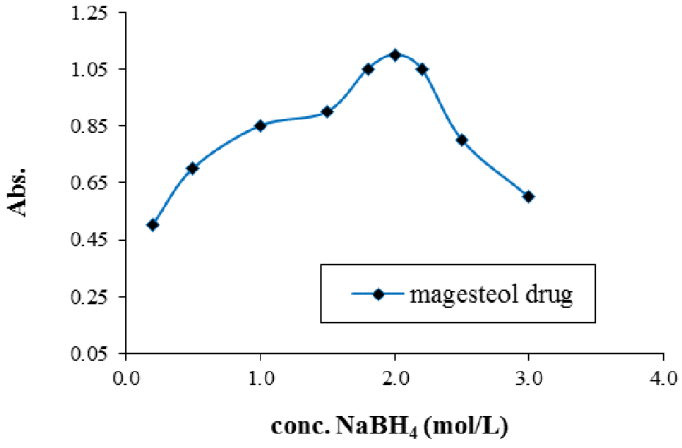

Figure. 7C. The impact of sodium borohydride, in the absorbance rate. (aqueous sample volume, 10 mL: *Origanum majorana*-capped AgNPs, 2.0×10^{-2} M, pH =5, megestrol drug = 10.0 μgL^{-1}, time 8 min, 345 nm).

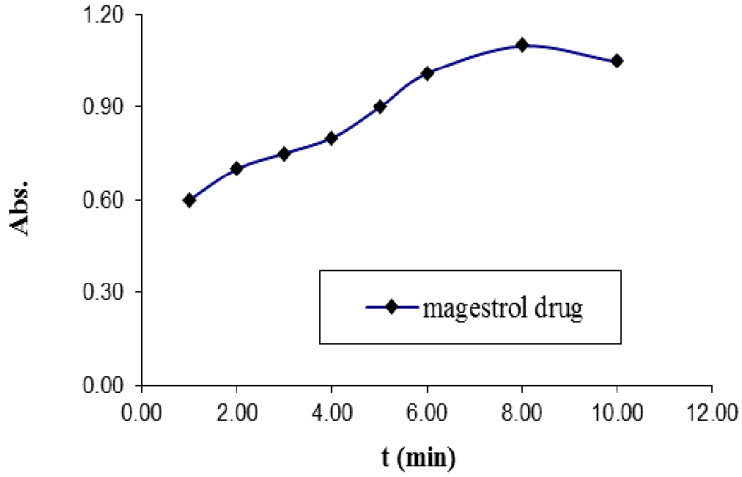

Figure. 7D. The impact of time in the absorbance rate. (aqueous sample volume, 10 mL: *Origanum majorana*-capped AgNPs, 2.0×10^{-2} M, sodium borohydride, 2.0×10^{-3} M, pH =5, megestrol drug = 10.0 μgL^{-1}, 345 nm).

Effect of ionic strength

In order to study the absorbance kinetic Spectrophotometric effect the experiments were carried out by adding different salts such as KCl, NaCl and K_2SO_4 The results indicate that the addition of up to 5.0 $\mu g\ L^{-1}$ of K_2SO_4 and 0.5 $\mu g\ L^{-1}$ of NaCl, KCl did not have any significant effects on the. In the high concentration, it was observed that the megestrol drug of the sample solution is close to the drug of blank solution was decreased [29]. However, it is possible that sensor could change the surface of *Origanum majorana*-capped AgNPs sensor. So that in the high concentration of sensor, interaction between megestrol drug and *Origanum majorana*-capped AgNPs sensor decreased and thus aggregation decreased.

Response time

As is known, the response time (t98.5 %) of a sensor, the time required for the response of the sensor towards a certain concentration of the measured ion to reach (98.5%) of its final value (steady state). Controlling the response time of the membrane is attainable via checking the needed time for the analyte to disperse from the volume of the solution to the *Origanum majorana*-capped AgNPs interface and to connect with the megestrol medicament solution. Through registering the change in absorbance intensity (at from pH=5 in 345 nm) to megestrol medicament solution of (10.0 μgL^{-1}), the response time of the present membrane was examined. As evident in (Fig.8), it is revealed that the *Origanum majorana*-capped AgNPs reached (98.5%) of the final signal at (1min at 12 min) contingent upon the time, is one of the predominant parameters that must be determined experimentally, the time-dependent response.

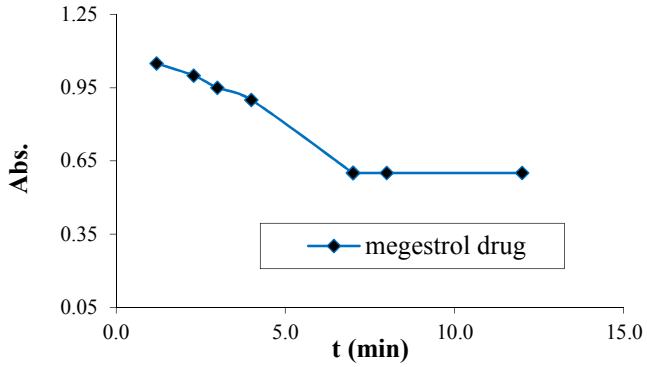

Figure 8. Typical response curve of the *Origanum majorana*-capped AgNPs at (345 nm) as a function of time when film was exposed to (10.0 μg L^{-1}) megestrol drug**.**

Measurement of megestrol drug in standard solutions and calibration

Analytical performance of *Origanum majorana*-capped AgNPs sensor for determination of megestrol drug under the optimum condition was recorded for different concentration of megestrol drug onto the *Origanum majorana*-capped AgNPs. The absorbance kinetic Spectrophotometric peaks with linear range of (0.01–12.0 μgL^{-1}) for megestrol drug were obtained respectively [23,30]. The linear regression equations of megestrol drug and coefficients of determination was y = 1.282C + 0.4622 (R^2 = 0.9903), respectively (Fig. 9). LOD of the modified *Origanum majorana*-capped AgNPs sensor and megestrol drug was calculated based on three times of standard deviation of the blank signals to calibration slope (3S/m). LODs were calculated (0.023 μgL^{-1}) of megestrol drug, respectively. For individual determination of each analyte, the concentration of megestrol drug was kept constant in (10.0 μgL^{-1}) while concentration of megestrol drug was changed from (0.01 to 12.0 μgL^{-1}) in (Figure 9).

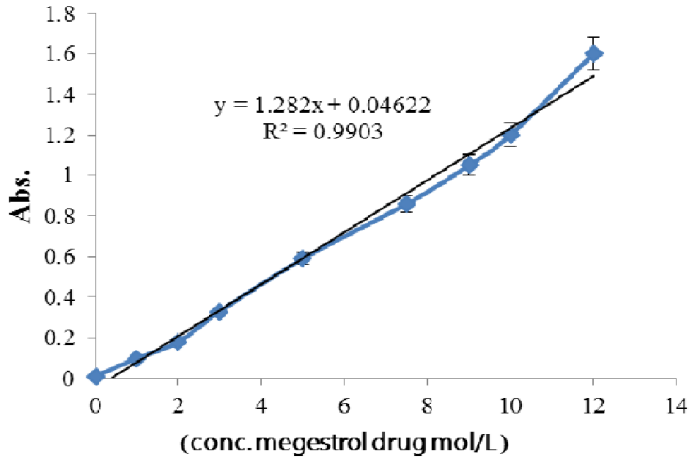

Figure 9. Calibration graph for megestrol drug. (aqueous sample volume, 10 mL: *Origanum majorana*-capped AgNPs, 2.0×10^{-2} M, sodium borohydride, 2.0×10^{-3} M, 345 nm).

Optimum values of parameters

The optimum values of parameters are demonstrated in Table 1. The method can be used as an alternative method for megestrol medicament measurement owing to advantages like excellent selectivity and sensitivity, low cost, simplicity, low detection limit and no need in utilizing organic harmful solvent.

Table 1. Investigation of method repeatability at conditions.

Parameter	Optimum Value for Megestrol drug
Megestrol drug (M)	(10.0 µg L^{-1})
Origanum majorana-capped AgNPs (M)	(2.0×10^{-2} M)
concentration $NaBH_4$ (M)	(2.0×10^{-3} M)
pH	5.0
Equilibration time (min)	(8.0 min)
Linear range (LDR)	(0.01 - 12.0 µg L^{-1})
Detection limit (LOD)	(0.023 µg L^{-1})
Relative Standard Deviations (RSD)	(1.8%)
Accuracy and precision	High
Advantages	High repeatability, sensitivity, selectivity, wide linear range and no need to organic solvent

Interference studies

After establishing the measurement method, to evaluate the selectivity of the prepared *Origanum majorana*-capped AgNPs sensor for determining the megestrol medication, the effect of the interaction of different other medications, molecules and ions in determining the megestrol medication was investigated. The considered limit was considered as the concentration of the annoying species that caused the change intensity of analyte adsorption, more than (5%) of the initial value. To determine the degree of interference of each species in the measurement of (10.0 µg L^{-1}) solution of megestrol medication, so much was added to this solution of the disturbing species that its absorption intensity changed by 5% compared to the initial absorption intensity [31]. The results are shown in Table 2. The results showed that most of the other medications under study did not have much effect on the measurement of megestrol drug and among them, compounds with a more similar structure or with more functional groups are more disturbing, which it may be related to their hydrogen interactions or the molecule of the megestrol drug and thus reduce the measurement of the megesterol medication in the analyte sample. As exhibited in (Table.2), the tolerance limit was determined as the max concentration of the interfering substance which

resulted in an error less than (±5%) for determination of megestrol medicament. The So selectivity of the recommended method was proven.

Table 2. Impacts of the matrix medicaments on the retrieving of the examined megestrol drug (N=6).

Drugs	**Effects of the matrix drugs (mg L^{-1})**
Amoxicillin, Ampicilline, Acetominophene, Cyclosporine	1000
Tramadol, Methadone	800
Naratriptan, Rizatriptan, Sumatriptan, and Zolmitriptan	250
Sulfacetamide	100

Application of the real sample

In order to evaluate the efficiency of the proposed sensor for determining megestrol drug in real samples, this *Origanum majorana*-capped AgNPs sensor was used to measure megestrol medication in urine and blood human samples according to the instructions mentioned for megesterol medication experiment 7 replicates measuring section [32]. The obtained percentage percentiles in (Table 3), indicate that the prepared sensor has a very good performance for determining the drug megestrol medication in urine and blood human samples. Therefore, In all real and synthetic sample amount of megestrol drug was found by standard addition method. The level of the megestrol medicament was estimated to be below the detection limit of related element. Based on the outcomes of replicating analyses for each sample, it was shown that the medication retrievals were mainly quantitative with a low RSD [33]. The potentiality of the recommended method for the determination of trace quantities of these elements in distinct samples was proven.

Table 3. Retrieval of trace megestrol medicament from urine and blood samples after applying presented procedure (N=6).

Samples	Added (µg mL^{-1})	Founded (µg mL^{-1})	RSD %	Recovery %
Urine hospital Ahvaz	0.00	0.30	2.6	----
	0.10	1.28	1.5	98.9
Blood hospital Ahvaz	0.00	0.42	1.1	----
	0.10	1.41	1.4	103.0
Urine hospital Shiraz	0.00	0.28	3.7	----
	0.10	1.31	2.8	102.0
Blood hospital Shiraz	0.00	0.50	3.8	----
	0.10	1.53	3.0	98.0
Urine hospital Boushehr	0.00	0.32	2.6	----
	0.10	1.34	3.2	101.2
Blood hospital Boushehr	0.00	0.67	2.5	----
	0.10	1.64	2.1	101.7

Comparison of results for this work with other reported sensors

In order to illuminate the applicability and efficiency of biosensor in this work, the results are compared with those of some of the recently reported methods for the reduction of variety of materials by sensor in (Table 4). Obviously, *Origanum majorana*-capped AgNPs shows the shortest time for the reduction of drugs in comparison with literature other sensors.

Table 4. Comparison of results for this work with other reported sensors.

Samples	Sensor	Time	References
Megestrol drug	polymer (MASDs)	15.0 min	7
Megestrol drug	Biopolymer (Rofam 70: a rapeseed methyl ester ethoxylate)	15.0 min	9
Sulfacetamide drug	Starch-capped AgNPs	7.0 min	23
Methyl orange	Seashell -capped AgNPs	11.0 min	34
Methyl orange	Ag/TiO_2 nanocomposite	9.0 min	35
Methyl paraben and propyl paraben	*Albizia Lebbeck Leaves*-capped AgNPs	60.0 min	36
Ni^{2+} and Co^{2+} ions	*Origanum majorana*-capped AgNPs	65.0 min	21
Parabens dye	*Origanum majorana*-capped AgNPs	60.0 min	37
Megestrol drug	*Origanum majorana*-capped AgNPs	8.0 min	Present study

Conclusion

In this work, AgNPs, and *Origanum majorana*-capped AgNPs were synthesized using sodium borohydride extract as reducing and stabilizing agents. A successful analytical method for measuring megestrol medicament was prosperously developed via utilizing a sensitized spectrophotometric with the help of *Origanum majorana*-capped AgNPs. The method can be used as an alternative method for megestrol medicament measurement owing to advantages like excellent selectivity and sensitivity, low cost, simplicity, low detection limit and no need in utilizing organic harmful solvent or extraction. The reaction was evaluated by measuring the absorption rate of megestrol drug, the optimum conditions. Which strongly confirms the greater contribution for the deletion of megestrol drug by *Origanum majorana*-capped AgNPs sensor. On the other hand, some of advantages for this work are listed below:

(I) *Origanum majorana* plant is very inexpensive, energy saving, and the most important of all non-toxic

(II) Fast and clean synthesis without the use of hazardous, toxic and dangerous compounds or surfactants as a highly stable and reusable eco-friendly catalyst under solvent-free condition

(III) Origanum majorana-capped silver nanoparticles sensor provides several advantages such as simple, mild condition, easy workup, and excellent yield in a short time.

(IV) The use of sodium borohydride extract as an economic and effective reducing and stabilizing agent

(V) The use of waste *Origanum majorana*-capped AgNPs sensor as a natural and inexpensive valuable resource and environmentally benign support

All these characteristics make *Origanum majorana*-capped AgNPs sensor a potential biosensor for drug measurement when juxtaposed against other commercial materials

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Conflict of interest

The authors declare that they have no conflict of interest related to the publication of this article.

References

[1] P.A. Meaney, V.M. Nadkarni, K.B. Kern, J.H. Indik, H.R. Halperin, *Crit. Care. Med.,* 38, 10 (2010).

[2] J.P. Sylvestre, M.C. Tang, A. Furtos, G. Leclair, M. Meunier, J.C. Leroux, *J. Contr. Rel.,* 149, 273 (2011).

[3] Y.P. Shiu, Y.M. Tang, X.F. Zhang, J. Ge, Z.C. Pu, *Bangladesh. J. Pharmacol.,* 10, 383 (2015).

[4] Y. Yamini, M. Tayyebi, M. Moradi, A. Vatanara, *Thermochim. Acta.,* 569, 48 (2013).

[5] C. Madeddu, M. Dessi, F. Panzone, R. Serpe, G. Antoni, M.C. Cau, L. Montaldo, Q. Mela, M. Mura, G. Astara, F.M. Tanca, A. Maccio, G. Mantovani, *J. Clin. Nutr.,* 31, 176 (2012).

[6] K. Jang, S. Yoon, S.E. Kim, *Drug. Des. Devel. Ther.,* 8, 851 (2014).

[7] S.W. Hong, B.S. Lee, S.J. Park, *Arch. Pharm. Res.,* 34, 127 (2011).

[8] Y. Pu, F. Cai, Z. Wu, D. Wang, X. Wen, Y. Li, J.F. Chen, X. Chen, N.R. Foster, *J. Chem. Eng. Data.,* 62, 1139 (2017).

[9] M. Lachowicz, M. Kolodziejczyk, M. Lukosek, P. Olszewska, P. Szymanski, *Molecules,* 21, 197 (2016).

[10] E.S. Ha, J.S. Kim, I.H. Baek, J.W. Yoo, Y. Jung, H.R. Moon, M.S. Kim, *Drug. Des. Dev. Ther.,* 9, 4269 (2015).

[11] N. Fakhari, S. Abbasian, A. Moshaii, M. Nikkhah, *J. Colloida. Surf. B. Biointerfaces,* 148, 657 (2016).

[12] A. Syafiuddin, M.R. Salmiati, A.B.H. Kueh, T. Hadibarata, H. Nur, *J. Clin. Chem. Soc.,* 64, 732 (2017).

[13] X. Fang, H.X. Ren, H. Zhao, Z.X. Li, *J. Microchim. Acta.,* 184, 415 (2017).

[14] B. Sadeghi, A. Rostami, S.S. Momeni, *Spectrochim. Acta. A.,* 134, 326 (2015).

[15] F. Shahrouei, S. Elhami, E. Tahanpesar, *J. Spectrochim. Acta. A. Mol. Biomols. Spectrosc.,* 203, 287 (2018).

[16] X.F. Zhang, Z.G. Liu, W. Shen, S. Gurunathan, *Int. J. Mol. Sci.,* 17, 1534 (2016).

[17] A.C. Burduşel, O. Gherasim, A.M. Grumezescu, L. Mogoanta, A. Ficai, E. Andronescu, *Nanomaterials,* 8, 681 (2018).

[18] Z. Kazemi, F. Marahel, T. Hamoule, B. Mombini Godajdar, *J. Phys. Theor. Chem.,* 16(3,4), 75 (2019).

[19] C.M. Kaye, M.J. Sankey, L.A. Thomas, *J. Clin. Pharmacology,* 9, 528 (1980).

[20] A. Shokrollahi, H.E. Haghighi, E. Niknam, K. Niknam, *J. Quim. Nova. Sao. Paul.,* 36, 273 (2013).

[21] Z. Kazemi, F. Marahel, T. Hamoule, B. Mombini Godajdar, *J. Desal. Water. Treat.,* 213, 381 (2021).

[22] A. Hatamie, F. Marahel, A. Sharifat, *Talanta,* 176, 518 (2018).

[23] M. Pargari, F. Marahel, B. Mombini Godajdar, *J. Phys. Theor. Chem.,* 17(1,2), 1 (2020).

[24] C. Krishnaraj, E.G. Jagan, S. Jagan, P. Rajasekar, P.T. Selvakumar, N. Kalaichelvan, *J. Colloids. Surfaces B : Biointerfaces,* 76, 50 (2010).

[25] A. Dehghanpoor Frashah, S. Hashemian, F. Tamadon, *Eur. J. Anal. Chem.,* 15, 32 (2020).

[26] M.A. Karimi, M.A. Mozaheb, A. Hate-Mehrjardi, H. Tavallali, A.M. Attaran, G. Deilamy-Rad, *J. Scientia. Iranica. Trans. F. Nanotechnology,* 22, 2736 (2015).

[27] C. Taniguchi, Y. Kawabata, K. Wada, S. Yamada, S. Onoue, *Expert. Opin. Drug. Deliv.,* 11, 505 (2014).

[28] M. Zohreh, S.M. Ghoreishi, M. Behpour, M. Mohammad Hassan, *Arab. J. Chem.,* 10, 657 (2017).

[29] S.M. Hejazi, M. Erfan, S.A. Mortazavi, *Iran. J. Pharm. Res.,* 12, 239 (2013).

[30] E. Keskin, S. Allahverdiyeva, E. Şeyho, Y. Yardim, *J. Serb. Chem. Soc.,* 84, 1 (2019).

[31] Z. Masoudyfar, S. Elhami, *J. Spectrochim. Acta. A. Mol. Biomol. Spectrosc.,* 211, 234 (2018).

[32] H.S. Wen, X. Li, Y.Z. Cao, C.C. Zhang, F. Yang, Y.M. Shi, L.M. Peng, *Chemotherapy,* 58, 461 (2012).

[33] Z. Jafariazar, N. Jamalinia, F. Ghorbani-Bidkorbeh S.A. Mortazavi, *Iran. J. Pharm. Res.,* 14, 23 (2015).

[34] A. Rostami-Vartooni, M. Nasrollahzadeh, M. Alizadeh, *J. Colloid Interface Sci.*, 470, 268 (2016).

[35] M. Atarod, M. Nasrollahzadeh, S.M. Sajadi, *J. Colloid Interface Sci.*, 462, 272 (2016).

[36] F. Maghami, M. Abrishamkar, B. Mombini Godajdar, M. Hosseini, *Desal Water Treat.,* 228, 389 (2021).

[37] N. Karachi, S. Motahari, S. Nazarian, *Desal Water Treat.,* 228, 389 (2021).