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Determination of small amounts of fluoxetine in a biological sample through solid phase extraction method by carbon nanotubes

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The entry of drugs produced into nature causes many environmental problems, which shows the importance of controlling and measuring these drugs more than before. Due to the importance of this measurement, some environmental laboratories are dedicated for improving a method to determine small amounts of fluoxetine as pollutant in water and a biological sample. In this research study, new techniques were applied for solid phase extraction of insignificant amounts of fluoxetine in water samples by carbon nanotubes and its measurement with ultraviolet-visible spectroscopy in biological samples. These techniques are two-phase systems in which donor phases are fluoxetine-containing aqueous samples and acceptor phases are amino-functionalized carbon nanotubes. The experiments were carried out in two stages of extraction from desolate water samples of fluoxetine using methanol as solvent and the desolate samples were taken to UV-Vis spectrophotometer for further analysis. This method is inexpensive, simple and fast, and is consistent with many of the existing machine methods. Extraction parameters such as the effect of desolating organic solvents, pH of donor and acceptor phases, extraction time, desolation time, mixing speed, volume of donor phase and surfactant effect were optimized and quantitative investigations and measurements were done under optimum conditions. The aforementioned techniques have many advantages including short extraction time, low consumption of organic solvents, deleting the effect of previous experiments, low detection limit, and high concentration factor. Concentration factor and detection limit for fluoxetine were found to be 14.3 and 13.6 µg, respectively.

KEYWORDS

Fluoxetine; amino-functionalized carbon nanotubes; spectrophotometry.

Introduction

Solid phase extraction is derived from conventional chromatography in which an adsorbent medium is used to isolate the samples based on the difference in balance with the adsorbent medium [1-6]. These benefits include quick analysis, easy process, possibility to automate work steps, analysis of very small amount of analyze, concentration and purification of samples, possibility to store and transfer samples from the site, sampling to analysis location, use of small volumes of organic solvents which are mostly poisonous. Some measurement methods used for fluoxetine are mentioned below. Antonio

Philip et al. developed the two-phase liquid-phase micro-extraction method using a hollow fiber with an injection duct, and gas chromatographic analysis was developed for the extraction and detection of Fluoxetine (FLX) and Norfluoxetine (N-FLX) in human plasma. Under the favorable conditions, the linear method is proposed at the range of 10-500 ng/mL and (R^2=0.9973) for FLX and at the range of 15-500 ng/mL and (R^2=0.9972) for N-FLX. Relative standard deviation (RSD) was obtained between 4.8-13.1% and 5.4-14.2% [7-11]. Dixit *et al*. described a method for filtering and analyzing FLX and (N-FLX) using the column of solid phase extraction and gas chromatography with an electron absorption detector. The linear quantization curve for FLX and (N-FLX) is more than the range of 20-200 ng/mL. Total extraction efficiency is extraction processes, which are found to be more than 90% and 75% and with correlation coefficients of 0.997 and 0.993 for FLX and (N-FL) [7-9]. Anna Ribbro *et al.* used liquid chromatography system with high efficiency in microbial decomposition, which is the most important process for the removal of organic pollutants in wastewater treatment plants. The mobile optimization phase of liquid ethanol was ammonium acetate buffer (92/7:55, v/v) at pH=6.8 [12-16]. The linear curve was R^2=0.99, selectivity and sensitivity were in a wide range of 460 ng/mL for FLX enantiomers and 2-30 ng/mL for N-FLX enantiomers. The detection limit was between 0.8-2.0 ng/mL and the quantitative limitation was between 2-4 ng/mL for both FLX and N-FLX enantiomers of its active metabolite. The method was used successfully and it was proved that the destruction of both FLX enantiomers in the sample of wastewater was during 46 days [17-21]. Amer used step-by-step solid phase extraction method with liquid chromatography-electron ionization-mass spectrometry that is used to improve the sensitivity of determining the amount of fluoxetine hydrochloride in human plasma. The Method was confirmed at the range of 5-60 ng/mL FLX, and the correlation coefficient R^2=0.999. The relative standard deviation was between 8.5-11% and 6.6-7.5%, respectively [17-21]. Bagheri et al. developed a new method based on a combination of magnetic solid phase extraction (MSPE) and mass spectrometry for separation and pre-concentration of the FLX form in water samples and biological samples using sodium dossal sulfate (SDS). Fe_3O_4 particles were covered and used as absorbent. Under the optimization conditions, the method successfully extracted FLX from urine and water specimens and absolute recovery values was used from 85% of the detection limit of 20 µg/L and relative standard deviation (RSD) of 1.4%. The linear response was greater than a range of 50-1000 µg/L with R^2 = 0.9968. Relative improvement in various matrices of water and urine specimens was investigated and the values 80% to 104% were obtained [1, 22-25].

Single-wall nanotubes consist of cylindrical walls of 1 to 2 nm in diameter. The multi-wall type has thicker walls and is composed of several co-axial cylinders separated by a gap of 3 to 4 nm (in the distance between the graphite layers). When the graphite plates are interwoven, carbon nanotubes change into several concentric hollow cylinders. Multiwall nanotubes have an average diameter of 10 to 15 nm and a length of 10 to 50 nm. The outer diameter of multiwall nanotubes is 2 to 25 nm, and its inner hole diameter is at the range of 1-8 nm, and there is no three-dimensional order between the individual graphite layers. The average length of nanotubes can be several microns. This method is modified through the use of solid phase extraction of AMX by magnetic nanotube absorbent before determining spectrophotometry. AMX is examined by using a method based on the formation of an Azo color derived from this drug. Synthesized nanoparticles were identified using the TEM, XRD, and FT-IT measurement. In the next step, several factors that can potentially affect AMX absorption and

desorption were optimized. The results indicated that, under optimized conditions, it was possible to determine the sensitivity and selectivity of examined narcotics within the range of 0.1000-0.5 ng/mL (-1) with a detection limit of 0.3 ng/mL (-1). Furthermore, in the actual analysis sample (e.g. amoxicillin capsule and human urine specimen), the results showed that a reliable and promising method for determining AMX in the actual sample is examined [26-31].
In direct extraction of lead (II) by the return of human blood serum and the limited use of carbon nanotube and its determination by atomic absorption spectrometry, carbon nanotubes oxide with layers of bovine serum albumin led to the modification of restricted access carbon nanotubes (RACNTs). This material can directly extract lead (2+) from untreated human blood serum when all the proteins of serum are removed. Protein output capacity is nearly 100% and the maximum lead (+2) adsorption capacity is 34.5 mg, detection method is 2.1 µg L (-1), an enrichment factor of 5.5 as the relative standard deviation is less than <8.1%. the improvement of the sample polluted lead (2+) for the extraction from untreated human blood serum was considered in the time interval from 89.4% to 107.3%.

In this study, we are going to measure fluoxetine in real samples (blood plasma, urine) by the interaction between nano absorbent and drug through UV-Visible spectrophotometer. The method is based on the interaction between the drug and nano absorbent. Parameters affecting the interaction and those affecting the measurement will be examined.

Experimental

Chemicals and reagents

Fluoxetine were prepared from Darmstadt, Germany of Merck, Method and dried for a week over phosphorus pentoxide in a vacuum desiccator before use. Carbon nanotubes were prepared from the Merck. All the solutions were prepared with doubly distilled deionized water from Darmstadt, Germany of Merck. It was conditioned before use by suspending in 4 M nitric acid for 20 min, and then washed two times with water.

Synthesis of functionalized nanotubes with amine

0.5233 g of raw multi-walled carbon nanotubes was added to the solution of 1 to 3 (v) nitric acid and sulfuric acid. The resulting mixture was placed in an ultrasonic bath with a frequency of 40 KHz for 30 min, followed by a 24-h mixing of the reflux. The resulting product was washed with distilled water until pH under the filter reached to about 7. The separated solid phase was dried for 12 h at 60 ˚C and under vacuum. COOHMWCNT, generated in the second stage, was mixed with ethylene diamine (20 mL) and was placed in an ultrasonic bath (40 kHz) at 60 ˚C for 5 h. The resulting mixture was stirred at 60 °C for 24 h, and the membrane of the resulting solid was removed by filtration of 0.22 µm polycarbonate powder and then it was washed with methanol without water. The resulting solid was dried overnight in a vacuum, and consequently MWCNT-$NH_{2,}$ was obtained.

Instrumentation

Double beam ultraviolet-visible spectrophotometer, Model UV1700. These conditions are tabulated in. The pH measurements conducted using the Sartorius model PB-11.

Preparation of method

In this study, new techniques were used for solid phase extraction of small amounts of fluoxetine in water samples by carbon nanotubes and its measurement with UV-visible spectrometry in biological samples. The strategies were in two-stage frameworks in which benefactor stages are fluoxetine-

containing fluid examples and acceptor stages are functionalized carbon nanotubes. The tests are done in two phases of extraction from forlorn water tests of fluoxetine utilizing a suitable dissolvable and the ruined examples are taken to UV-Vis spectrophotometer for additional investigation. Extraction parameters such as the effect of desolating organic solvents, pH of donor and acceptor phases, extraction time, desolation time, stirring speed, volume of donor phase and surfactant effect were optimized and quantitative investigations and measurements are optimized and quantitative measurements and examinations are done under optimum conditions. Consequently, concentration factor and detection limit, linear amplitude, and relative standard deviation are obtained for fluoxetine. To prepare the mother solution of fluoxetine (500 $mg.L^{-1}$), 50 mg pure fluoxetine powder was weighed and poured in a volumetric flask of 100 mL and reached to the volume with disintegrated distilled water. The solutions required for fluoxetine were prepared by diluting the mother solution with disintegrated distilled water.

Initial test: effect of absorbent on fluoxetine extraction

To investigate the effect of amino or carboxylic carbon nanotube absorbent or on fluoxetine extraction, we first perform the following steps for fluoxetine. For each container, the buffer was added at the range of 2-10. One milliliter of the desired drug (with the concentration of 10 ppm) was taken for fluoxetine, 0.01 g amino-functionalized carbon nanotube absorbent, 1 ml buffer (at the range of 2-10) were poured in 50-mL flask and reached the volume with disintegrated stilled water. Then the stylish act was performed for 15 m, then it was centrifuged for 15 m, and passed through the syringe filters and finally the quantitative measurement of fluoxetine was performed. The same was done for carboxyl-functionalized carbon nanotube absorbent. The quantitative measurement of filtered solutions for fluoxetine at a wavelength of 200 to 800 nm was done by two-beam UV-Vis device (Figure 1).

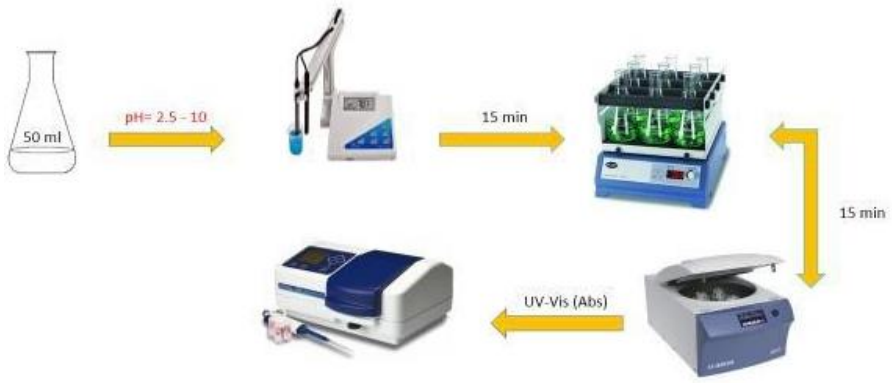

FIGURE 1 The desired drug along with amino-functionalized carbon nanotube absorbent and the buffer range of 2-10 was measured quantitatively by UV-Vis device after centrifugation.

Optimizing Wavelength in Fluoxetine Extraction

Effect of pH on fluoxetine extraction

To evaluate the effect of pH on the fluoxetine extraction, we first performed the following steps for fluoxetine. For each container, the desired tampon has been added, because the goal is to determine appropriate pH. One ml of the drug was taken (at a concentration of 10 ppm for fluoxetine), 0.01 g of amine adsorbed, 1 mL of buffer (in the range of 2-10), were taken and poured in a 50-mL flask and reached

to the volume with disintegrated distilled water. Then the stylish act was done for 15 minutes, and it was centrifuged for 15 min, passed through the syringe filters, and finally the quantitative measurement of fluoxetine was performed. The quantitative measurement of filtered solutions for fluoxetine at a wavelength of 231 nm was done by two-beam UV-Vis device.

Adsorbent rate effect

Another important parameter that affects the intensity of absorption is the rate of adsorbent. At this stage of testing, according to the previous stages, optimum pH and optimum adsorbent in the optimum wavelength were used according to the previous conditions and various amounts of adsorbent 5-10-15-20-30-40 mg were used.

Salt effect

Another important parameter is salt, which in practice acts as a pair of ions between reactive substances, makes the compounds react better, and is also very effective in adsorption intensity. At this stage of testing, according to the previous stages, optimum pH and optimum adsorbent in the optimum wavelength were used according to the previous conditions and various amounts of salt 10-20-30-50-70-100 mg were used.

Effect of the time of drug absorption in solution

Another important parameter on the absorption and measurement systems of the drug based on their extraction is the reaction speed. Seven Solutions were made at optimum conditions and the stylish act was done on them at different times of 5-8-10-15-20-28-35 m, then they were centrifuged and like previous steps, the solutions were passed through the filter and their absorption was read at maximum wavelength.

Effect of the type of desorption solvent

The type of desorption solvent is one of the most important parameters affecting the adsorption system greatly. In this study, solvents (methanol, ethanol, acetonitrile, acidic and basic methanol, acidic and basic ethanol) were assessed for fluoxetine, and the optimum solvent was selected for the drug. We collected 7 flasks of 50 mL, taking into account all the optimum conditions, then after each centrifugation, we removed the surface water of each container and added the solvents to them, then stylized them for 20 min and centrifuged them for 15 min. We filtered them and read their absorption at maximum wavelength (Figure 2).

FIGURE 2 Schematic of the quantitative measurement of fluoxetine and determination by UV-Vis spectrometry

Effect of desorption solvent volume

Another parameter that influences the absorption rate of the system is the volume of desorption solvent. In this study, different volumes of the selected solvent have been investigated. We added 5, 7, 10, 12, 15, 18 mL of desorption solvent to the isolated absorbent in optimum conditions and after styling for 20 min and centrifuging for 15 min. We read the absorbance value by UV-Vis device at the maximum wavelength.

Determining volume of concentration limit and factor

To get the limit volume, individual solutions in terms of the volumes of 50, 100, 150, and 200 mL were prepared for fluoxetine in optimized conditions.

Plotting the calibration curve of fluoxetine

After optimizing all the effective parameters in the absorption intensity, a calibration chart of the method was plotted. For this purpose, different concentrations of the drug were added to 50 mL volumetric flasks. Then, one percentage of 0.02 g of the sodium chloride salt was added to the fluoxetine and 0.02 g of amino-functionalized carbon nanotube absorbent and pH=10 was added to each of the flasks and reached the volume by adding disintegrated distilled water. Then the washing steps were done and the intensity of absorption of these solutions was read at the laboratory temperature for the drug and the calibration curve was plotted.

Limit of detection (LOD)

Generally, the limit of detection of an experimental compound is usually considered to be a concentration of it, with a device response that is significantly different from the control or field response. The Definition commonly used in analytical chemistry. Limit of detection is a concentration of an experimental compound with a response that is three times as much as the standard deviation of the control (S_b) and is obtained through the following equation.

$$LOD = \frac{3Sb}{m}$$

To obtain the detection limit of the method for measuring fluoxetine, four control solutions with optimal conditions but without adding drugs were prepared. Then, the intensity of absorption was read at the wavelength of each drug.

$$LOQ = \frac{10Sb}{m}$$

Precision of method

This parameter was used to verify test accuracy and proximity of study data. To evaluate the accuracy (in terms of relative standard deviation) the absorption intensity of 4 solution of fluoxetine was assessed in a day. For this purpose, four standard solutions with optimum concentrations were prepared in 50-mL volumetric flasks in very similar circumstances with the proposed methods.

Investigating the disturbing species and selectivity

The effect of an intrusive species on fluoxetine measurement was studied in terms of biological matrices under optimal conditions. For this purpose, the drug sample was mixed with different concentrations of disturbing species (the time of measurement is one hour after the addition of annoying species) and the absorption intensity in the absence of disturbing species was compared with a sample of the drug. The disturbing species of the ciprofloxacin was added with the concentration of 5, 10, and 15 ppm.

Preparation of plasma sample for the measurement of fluoxetine

Blood samples taken from humans were poured in tubes containing EDTA to the

volume of 2.5 mL. The samples were centrifuged for about 25 min with 3000 rpm. The yellow solution above the plasma tube was removed and to ensure that no protein was present in the plasma, 10 cc acetone was poured into 10 cc of the plasma and centrifuged for 5 min with 4000 rpm to deposit additional proteins. To measure with the proposed method, a certain volume of plasma was taken and the measurement steps were performed. The urine sample taken from human and filtered was stored in a black glass container. For measuring with the proposed method, a certain volume of the urine was taken and measurement was done.

Results and discussion

Investigating FT-IR, XRD and SEM spectra

The FTIR analysis results for the amino-functionalized sample are shown in Figure 3. As seen in Figure 3, the sharp peak observed in 3453 that refers to the N-H bond. The two peaks observed at the range of 2850-2960 nm represent the presence of C-H, which confirms that the amine group has been created on the nanotube. Moreover, the peak observed in 1031 is related to the C-H bending bonds, which further confirms the presence of the amine functional group Figure 3.

The peak of 3409 cm^{-1} represents the N-H stretch mode peak, according to Figure 4.

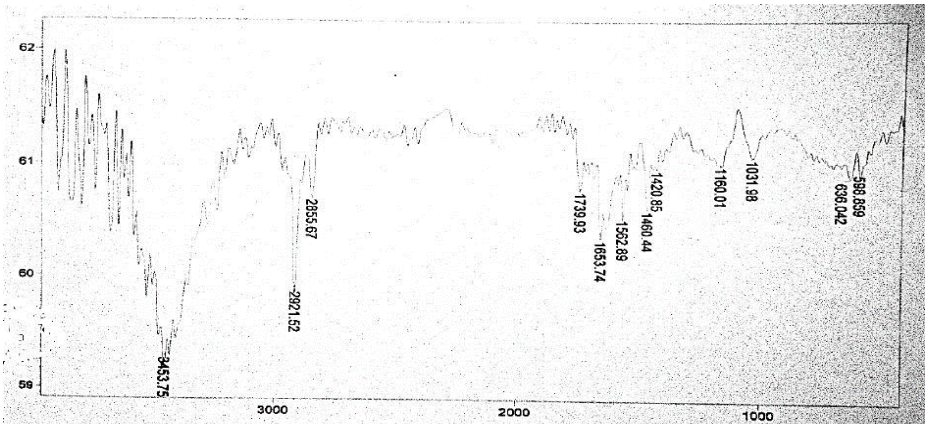

FIGURE 3 Infrared spectrum of carbon nanotubes containing amines before absorption in the CNT-Amine MW spectrum, a new peak is found in the area of 1620 cm^{-1}, which shows that the amine is successfully coupled to the outer surfaces of carbon nanotube

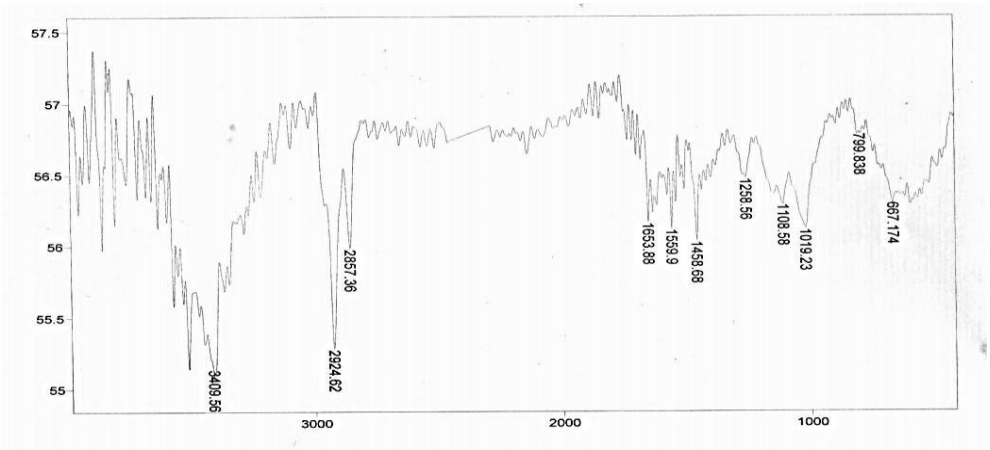

FIGURE 4 Infrared spectrum of carbon nanotubes containing amines after absorption Change in absorption is displayed in 3500cm^{-1}

To ensure the survival of the structure after functionalizing carbon nanotubes, the SEM images are shown in Figure 5.

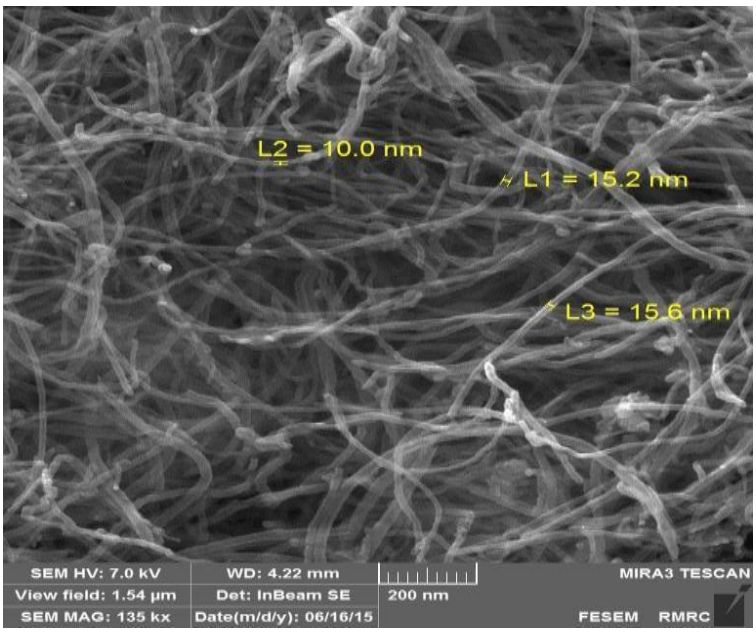

FIGURE 5 SEM of the structure of amine carbon nanotubes before absorption

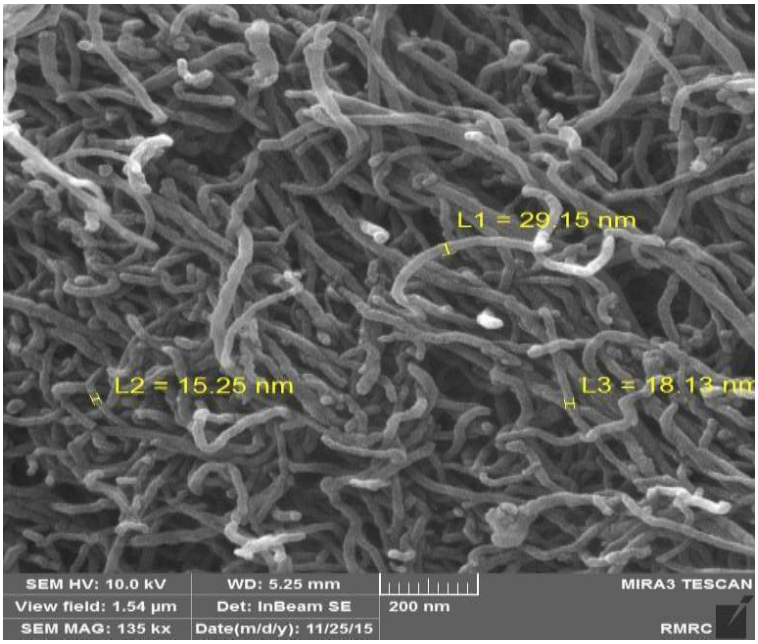

FIGURE 6 SEM of the structure of amine carbon nanotubes after absorption

Changes in the surface of amine carbon nanotubes represent the drug and increase the size of amine carbon nanotubes. From the SEM we can conclude that the thickness of the plates has increased. As seen in Figures 5 and 6, the functional amine group on the carbon nanotube surface is characterized by lighter spots, which indicating and confirming the absorption of the drug on the nanotubes (Figure 7 and 8). The Sheerer equation was used to determine the size of carbon nanotubes.

$$\tau = \frac{K\lambda}{\beta\cos\theta}$$

where τ is average crystallite size (in nanometers), K is crystal shape coefficient (usually 0.9), λ is tube wavelength producing X-ray (in nanometers), β is peak width, θ is the diffraction angle.

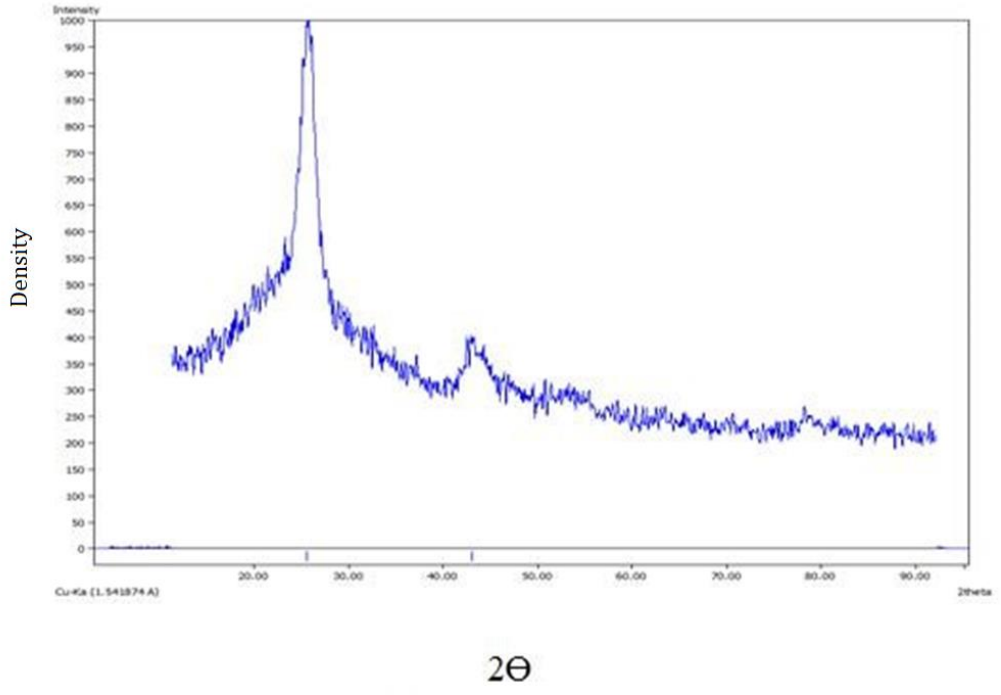

FIGURE 7 Analysis of XRD of amino-functionalized carbon nanotubes before adsorption

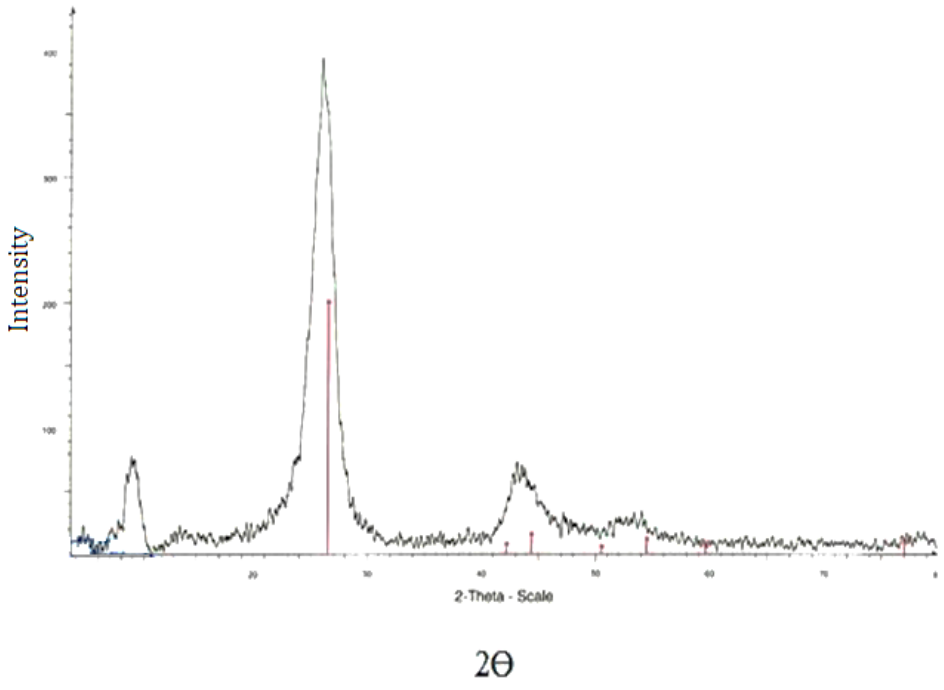

FIGURE 8 Analysis of XRD of amino-functionalized carbon nanotubes after adsorption. The change in intensity of 2Θ=260 represents the absorption of drug on amine carbon nanotubes

Effect of absorbent on fluoxetine extraction

As the target was to determine appropriate absorbent, the lowest amount of the absorbent was chosen as the best value Figure 9.

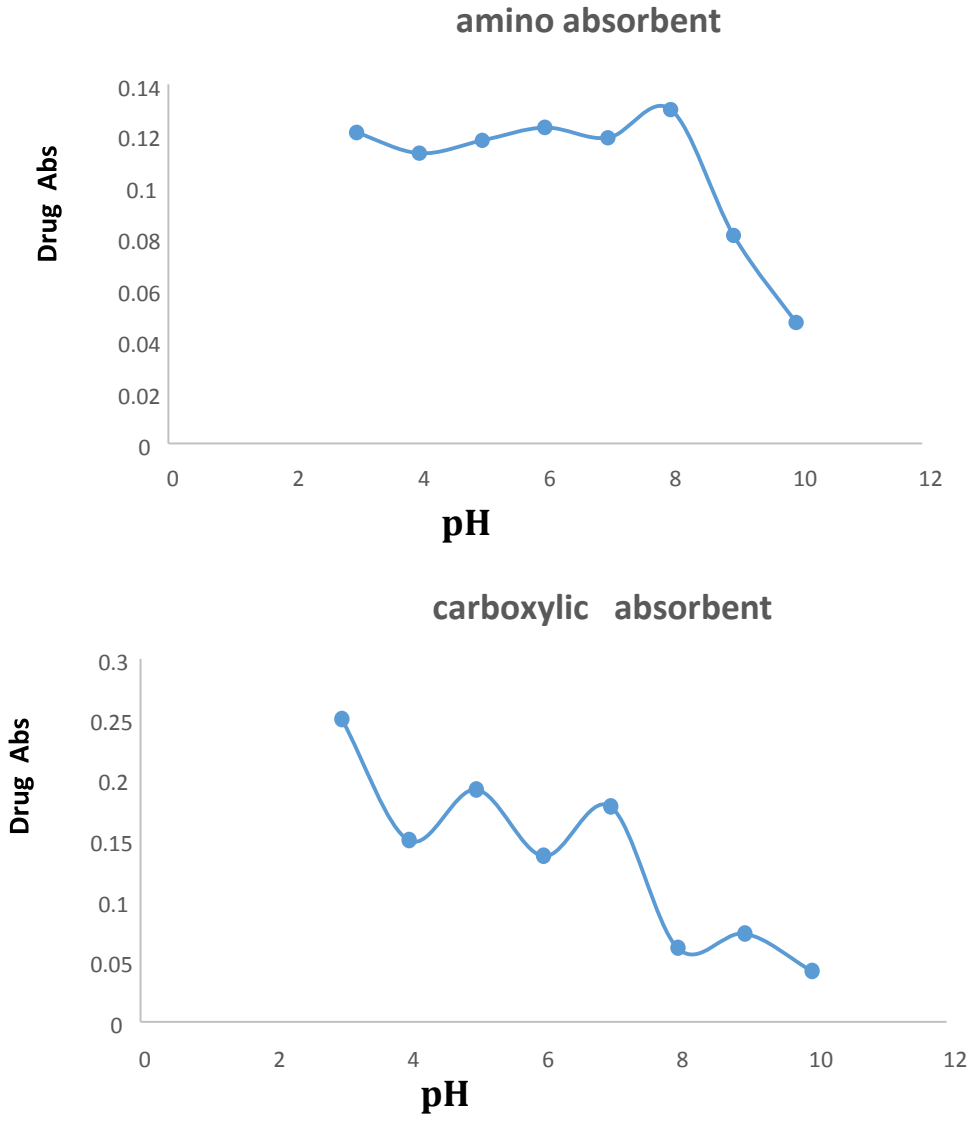

FIGURE 9 The curve of changes in the Fluoxetine absorption in relation with pH

According to the figure 9, the amino-functionalized carbon nanotube absorbent revealed a better absorption, and therefore amine was selected as the absorbent to extract the fluoxetine.

Optimizing wavelength in fluoxetine extraction

The desired drug along with the amino-functionalized carbon nanotube absorbent and the buffer at the range of 2-10 was measured quantitatively using the UV-Vis device after centrifugation. All of the spectra were coexisted at the wavelength of 231 nm, and the optimal absorption wavelength was also detected.

Effect of pH on fluoxetine extraction

To evaluate the effect of pH on fluoxetine extraction and since the goal is to determine appropriate pH, the lowest amount of the absorbent is chosen as the best value (at the abovementioned pH, the absorbent has the best conditions to absorb fluoxetine; thus the concentration of fluoxetine decreases in the sample, and that is why this pH is selected). The quantitative measurement of filtered solutions for fluoxetine at a wavelength of 231 nm was done by two-beam UV-Vis device.

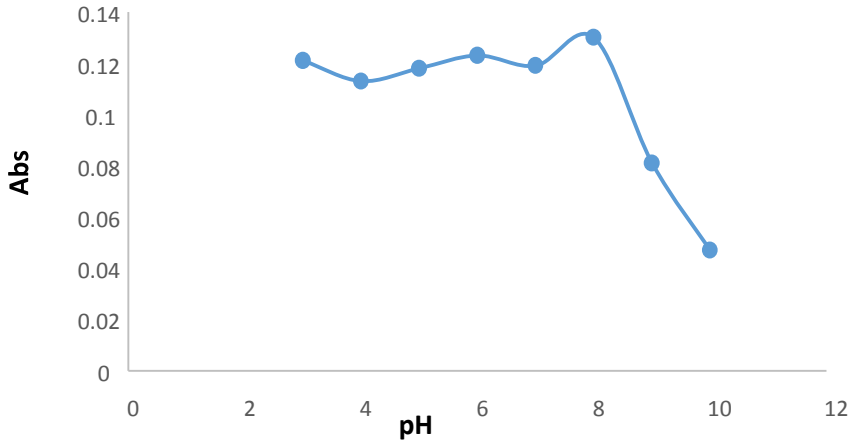

FIGURE 10 The effect of pH in the Fluoxetine absorption

The chart indicated that, with absorption at pH=10 for fluoxetine, suitable conditions are observed for the protonation of carbon nanotubes and that the highest fluoxetine absorption is on the amino-functionalized nanotube and electrostatically, the best conditions for the absorbent and drug for surface absorption is at pH equal to 10 radars.

Adsorbent rate effect

Another important parameter that affects the intensity of absorption is the rate of adsorbent. The diagram indicates that at lower amounts of absorbent, it is possible that some compounds enter the solution that can be absorbed at the maximum wavelength of the drug. The rate of the absorbent for the fluoxetine was selected to be 0.02 g.

Salt effect

Another important parameter is salt, which in practice acts as a pair of ions between reactive substances, makes the compounds react better, and is very effective in adsorption intensity. This graph shows that, by adding 0.20 gr of sodium chloride salt for fluoxetine extraction, the appropriate electrostatic charge is obtained on the adsorbent and the sample of the drug and in optimal conditions; the amount of salt was obtained as 2% $^{v}/_{w}$ for fluoxetine and displays the highest absorption of the drug.

Effect of the time of drug absorption in solution

Another important parameter on the absorption and measurement systems of the drug based on their extraction is the reaction speed. It indicated that, as the contact time between the absorbent and the drug increases, the conditions get better to achieve balance and then no change is made in the concentration of the drug in the solution. For fluoxetine, the optimal reaction time was selected to be 28 m to have the most suitable absorption.

Effect of the type of desorption solvent

The type of desorption solvent is one of the most important parameters affecting the absorption system greatly. We performed desorption and we chose the highest absorption due to the desorption.

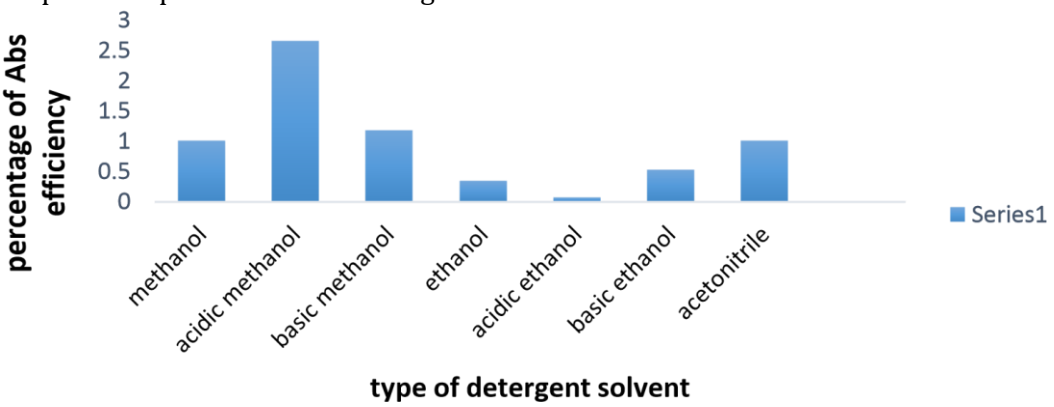

FIGURE 11 Effect of the type of desorption solvent

It suggests that in the equilibrium between the adsorbent and the desorption solvent, the best conditions are represented by acidic solvents. With regard to the highest absorbance for selecting the optimal solvent, acidic methanol was selected for fluoxetine.

Effect of desorption solvent volume

Another parameter that influences the absorption intensity of the system is the volume of desorption solvent. In this research study, different volumes of the selected solvent were assessed.

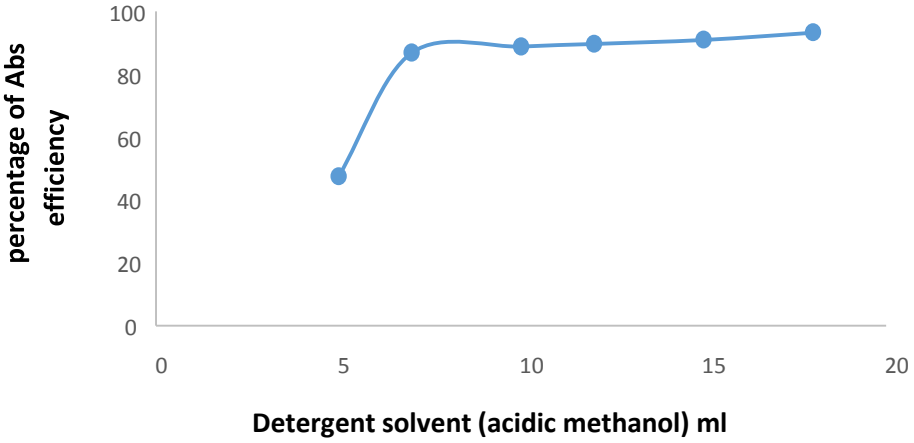

FIGURE 12 Desorption solvent volume

It shows that from the volume of 7 mL and more, the entire drug enters into the desorption solvent, and the balance goes quantitatively towards the desorption solvent and the desorption is completed. The optimum volume of desorption solvent for fluoxetine was chosen 7 mL.

Determining the volume of concentration limit and factor

To get the limit volume, individual solutions were prepared for fluoxetine in optimized conditions. According to the diagram, as the drug dilutes the possibility of full absorption on the absorbent decreases. As the result, the

volume of 100 mL was chosen for fluoxetine therefore calculate the Concentration Factor 14.3.

Plotting the Calibration Curve of Fluoxetine

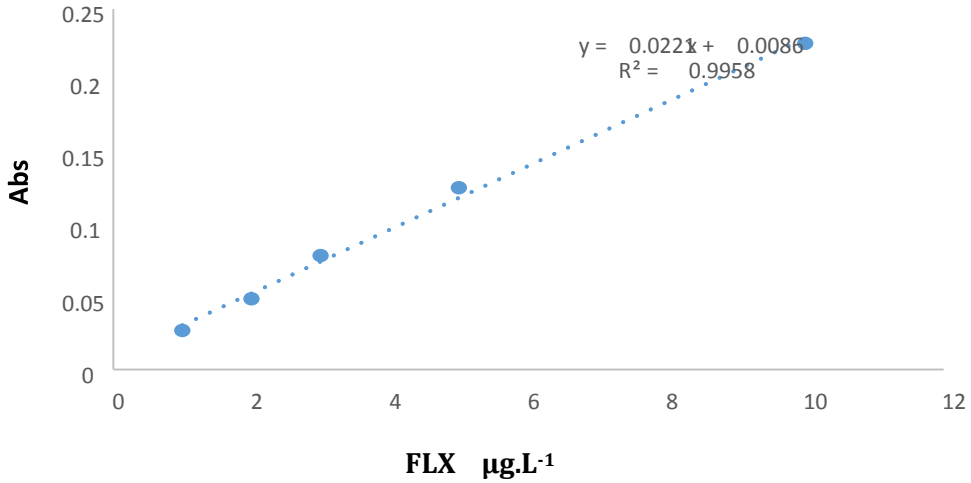

FIGURE 13 Calibration curve of fluoxetine

According to the obtained results, in optimum conditions, the absorption and concentration of drug in the concentration range is linear for fluoxetine.

Calculating Limit of Detection (LOD)

Considering that the slope of the calibration curve is 0/0086, The method's limit of detection (LOD) is obtained as follows:

S_b= 0.0001, C_{LOD} = 13.6 µg.L^{-1}

Using the above data, the LOQ was obtained using the Equation 5:

$$LOQ = \frac{10Sb}{m}$$

C_{LOQ} = 45.2 µg.L^{-1}

Precision of RSD%

This parameter was used to check the accuracy of the test and the appropriateness of the study data. By obtaining the absorption intensity at the maximum wavelength of each drug, RSD% was obtained in one day.

$$Sb=\sqrt{\frac{\Sigma(Ai-\bar{A})2}{n-1}}$$

$$\%RSD=S/m\times100$$

Standard deviation = 0.0031, mean = 0.030

%RSD = (S_b/m) ×100 → %RSD =% 3.33

Preparation of Biological Samples

Plasma and urine samples were taken to measure the fluoxetine by the proposed method and the measurement steps were taken. At this stage, we concluded that, the amount of the added drug is and the amount of the drug found in plasma and urine are the same, indicating that the accuracy of the method is acceptable Table 1. The effects of the intrusive species on fluoxetine measurements were studied with regard to biological matrices under optimal conditions. The disturbing type of ciprofloxacin is more disturbing at high concentrations (By diluting the absolute value of the annoying species decreases).

TABLE 1 Recovery of fluoxetine added to 1000mL of different water samples (pH= 10.0)

Sample	fluoxetine added (µg)	Fluoxetine determined (ng.mL^{-1})		Recovery
urine	0.0	1.78 (3.0)	ND	
	10.0	11.68(3.2)	11.2	96%
plasma	0.0	4.46(2.2)	ND	
	10.0	14.67(2.2)	14.3	98%

Values in parentheses are %RSDs based on five individual replicate analysis

Conclusion

In this study, a solid-phase extraction technique, ultraviolet-visible spectroscopy, preconcentration was used to measure amounts of fluoxetine in biological samples. The purpose of this research was to develop an efficient, selective, inexpensive and simple method for evaluating the amount of fluoxetine in biological samples. Development of the solid phase extraction method in recent years introduced an absorbent with efficient performance as a basic requirement. Therefore, in this study, amino functionalized carbon nanotubes were utilized as suitable adsorbents to increase the efficiency of fluoxetine extraction. The effective parameters on extraction such as pH, buffer type, buffer concentration, adsorbent amount, type and volume of solvent, reaction time, and salt effect were investigated. This method revealed good repeatability and wide linear range (1-10 mg.L^{-1}) and proper concentration factor for determining fluoxetine, and the linear range was found to be good with the detection limit of 13.6 µg.L^{-1}. The high repeatability was found to be one of the characteristics of this method. According to the results (Table 1), the advantage of this method compared to other methods is that the adsorbent used at high characteristic levels, which is a major factor in choosing this material for use as an adsorbent. The adsorbent used in the proposed method is able to recover, which can be tested extensively. Other advantages of the proposed method compared to other methods are lower detection limit, better concentration factor and simpler and easier technique compared to other methods.

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