4 Determination of captopril by fluorescence enhancement of 2MPA-CdTe nanocrystals probe

4.1 The photoluminescence changes of the 2MPA-CdTe nanoparticles caused by captopril

In this chapter, it is shown that the presence of captopril in non-buffered aqueous media causes the quenching of the photoluminescence measured from 2MPA–CdTe nanoparticles. On the other hand, in buffered systems, captopril effectively enhances the photoluminescence of quantum dots. The quenching was effectively described by modified Stern-Volmer model as ln (F_0/F) versus concentration of captopril (where F_0 is the photoluminescence of the nanoparticle dispersion in the absence of captopril and F is the photoluminescence measured from the nanoparticle system in the presence of captopril). The enhancement in photoluminescence of 2MPA-CdT quantum dots dispersion fits to a Langmuir model. The photoluminescence enhancement approach is analytically favoured due to its selectivity as compared to the luminescence quenching approach, therefore, it was used for the determination of captopril.

4.2 Optimization of the composition of the 2MPA-CdTe nanoparticles dispersion in non-buffered media for photoluminescence quenching

4.2.1 Influence of the pH

The hydrogenionic concentration of the aqueous medium plays a key role in the interactions between the analyte and the quantum dots [152]. The hydrogenionic concentration affects the aggregation of quantum dots and therefore the stability of these dispersions. Therefore, the photoluminescence from the aqueous dispersion of 2MPA-CdTe quantum dots was studied under different pH conditions. The results (Figure 28) indicated that the quantum dots exhibited

the highest photoluminescence signal at pH values of 7 and 8. As the pH (measured value) of the aqueous system was decreased (by the addition of HCl) or increased (by the addition of NaOH), the photoluminescence decreased until total quenching at pH values below pH 5 and above pH 10. In the acidic range, the photoluminescence from the dispersion is weak since the removal of the 2MPA capping occurs due to the protonation of the binding thiolates, which results in a large number of electron traps at the nanocrystals surfaces [153]. Moreover, in basic conditions, the photoluminescence intensity is enhanced as the carboxylic group of the 2MPA is deprotonated resulting in a homogenous density of negative charge that results in the better dispersion of nanocrystals. However, at pH 10, photoluminescence decreases due the formation of cadmium hydroxide at the quantum dots surface.

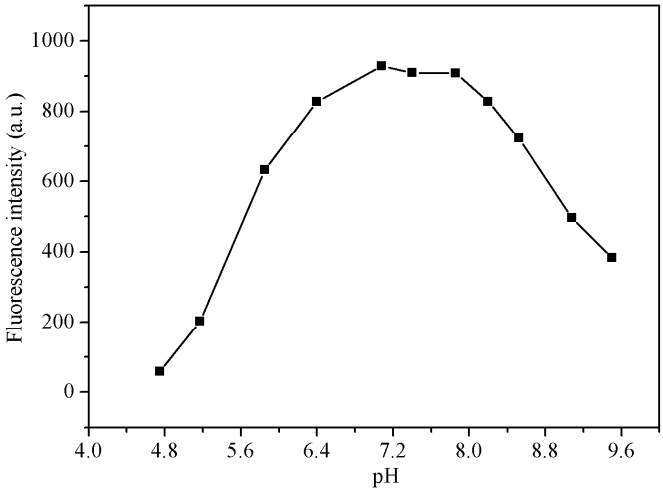

Figure 28 - Photoluminescence responses of aqueous quantum dots dispersions solution (2.8 x 10^{-8} mol L^{-1}) at different pH values adjusted by the addition of either 0.01 mol L^{-1} HCl or NaOH , excited at 350 nm and photoluminscence measured at 512 nm.

It is important to point out that captopril is not fluorescent when solubilized in aqueous solution and its molar absorptivity above 300 nm is close to zero. However as it is a weak acid affecting the pH of the aqueous solution (in a concentration dependent manner) as it has chemical groups (thiol and carboxylic acid) that present exchangeable protons. The results indicate (Figure 29) that after mixing captopril (1.5 x 10^{-5} mol L^{-1}) in the diluted aqueous dispersion, no changes

in florescence emission in alkaline media take place however, at neutral pH and acidic medium, the signal measured from the quantum dots are attenuated.

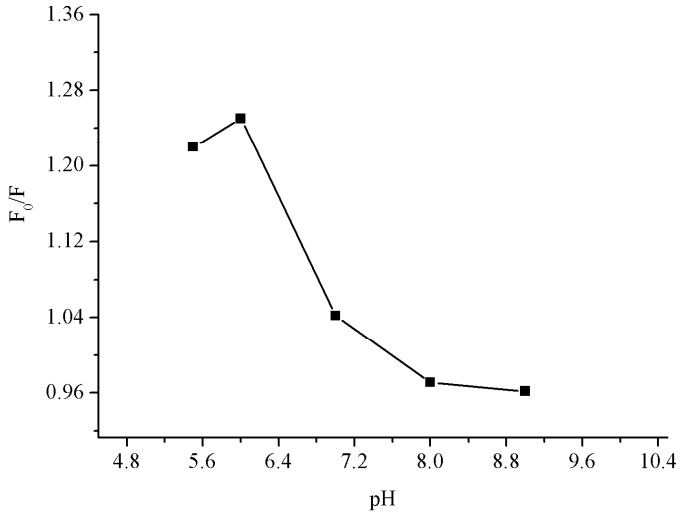

Figure 29 - Effect of pH value (adjusted either by 0.01 mol L^{-1} of HCl or NaOH) on the photoluminescence of 2MPA-CdTe quantum dots dispersion (2.8 x 10^{-8} mol per 1 L of solution) measured as F_0/F, where F_0 and F are respectively the photoluminescence of the quantum dots dispersion before and after the addition of 1.5 x 10^{-5} mol L^{-1} captopril.

4.2.2 Photoluminescence stability

The variation in photoluminescence intensity measured from the control dispersion of quantum dots in non-buffered aqueous dispersions was studied in function of the time (measured every 5 min up to 60 min at room-temperature) as indicated in Figure 30. The result demonstrated that the signal measured from the quantum dots dispersion is stable up to 25 min. After this time, variation takes place and photoluminescence intensity decreases 18% with respect to initial intensity after 60 min.

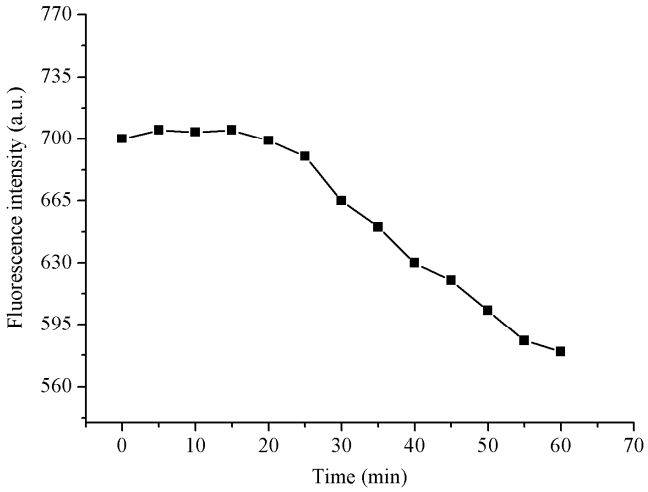

Figure 30 - Stability studies of the photoluminescence emission intensity of the quantum dispersion (control) as function of time.

The variation of the photoluminescence in aqueous 2MPA-CdTe dispersion in function of the time was also evaluated after mixing captopril (2×10^{-5} mol L^{-1}) in the quantum dots dispersion. Photoluminescence was measured every 5 min at room-temperature. The photoluminescence of the 2MPA-CdTe quantum dots decreased steeply in the first 5 min, stabilizing after 25 min after the addition of captopril. From that point, the photoluminescence was found to be stable up to at least 60 min (less than 5% random variation of signal) as indicated in Figure 31. Therefore, in order to obtain reliable quantitative measurements using the quantum dot dispersion, it was established that photoluminescence acquisition must be made in the interval between 15 and 25 min.

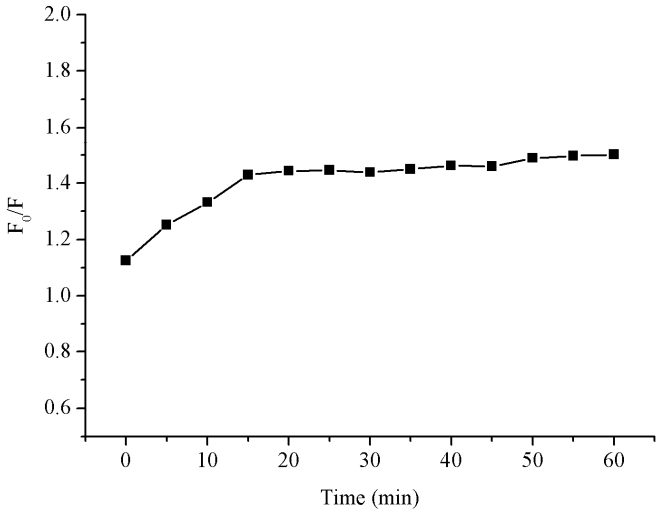

Figure 31 - Stability of the photoluminescence of the 2MPA-CdTe quantum dots dispersion after mixing captopril (2 x 10^{-5} mol L^{-1}).

4.2.3 Interactions of 2MPA-CdTe quantum dots with captopril under optimized condition in non-buffered aqueous media.

In order to understand and establish a response model for the quantum dots in the presence of captopril, aliquots of a captopril standard solution were added in order to cover final concentrations in the range between 8 x 10^{-6} and 7 x 10^{-5} mol L^{-1}. These additions were made to volumetric flasks containing the working dispersions of quantum dots. Photoluminescence was measured 15 min after the addition and mixing of captopril. As it is a weak acid in aqueous solution, partial ionization occurs, and the release of protons (pK_a 3.7 of the carboxylic group and pK_a 9.8 of the thiol group) affects the pH of the system [154]. The variation in the hydrogenionic concentration can be related with the concentration of the captopril present in aqueous dispersion of quantum dots. As expected, it was found a captopril concentration exponential-like dependency upon the photoluminescence emission from the dispersion of quantum dots, expressed as F_0/F, which is the ratio between the photoluminescence from the dispersion of quantum dots in absence of captopril (F_0) and the photoluminescence measured in the presence of captopril (F) as indicated in Figure 32. In order to adjust the photoluminescence

quenching model in a linear behavior, a calibration model was prepared using the ln (F_0/F) in function of the captopril concentration (Figure 33). As the concentration of captopril increased, no shift in the maximum emission wavelength occurred (see Figure 34), which indicated that there is no complex formation between captopril and the quantum dots.

In addition, due to the lack of significant absorption of captopril in the 300-700 nm range, the quenching cannot be attributed to inner-filter effect. In fact, after the addition of aqueous solution of captopril, the increasing hydrogenionic concentration causes the removal of 2MPA from the surface of quantum dots due the protonation of surface thiolates. The dissociation of 2MPA from the surface of nanoparticles at lower pH values (pH $\geq$ 7.0) result in lower charge density and the bare quantum dots tends to aggregate. The result is the severe photoluminescence quenching of the quantum dots dispersion [152].

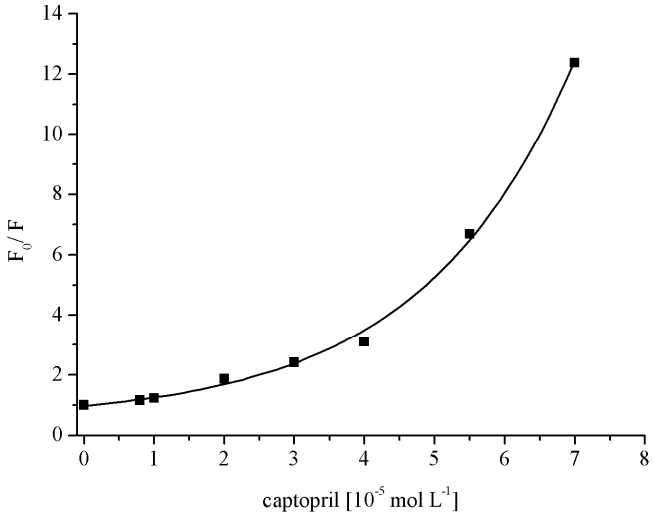

Figure 32 - 2MPA-CdTe quantum dots photoluminescence quenching non-linear model in function of the concentration of captopril

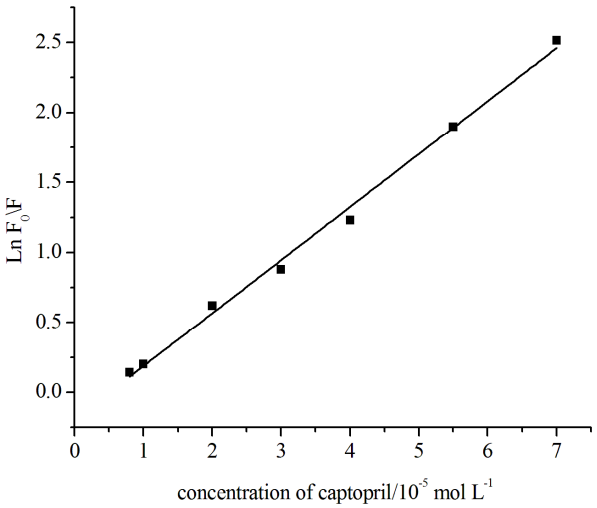

Figure 33 - 2MPA-CdTe quantum dots photoluminescence quenching linear model in function of the concentration of captopril.

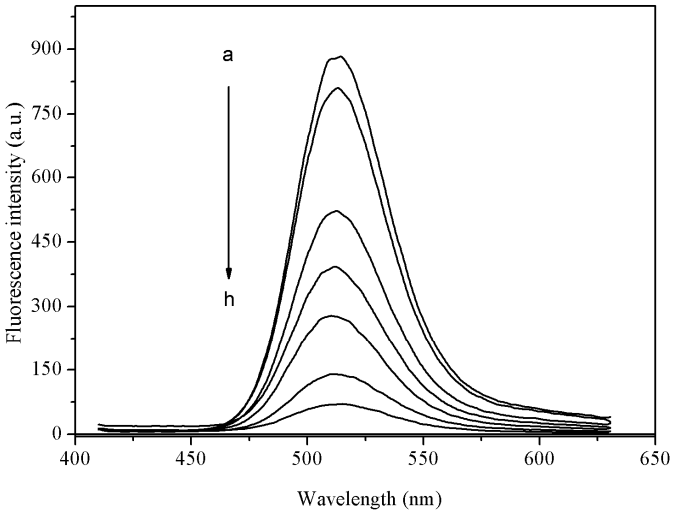

Figure 34 - Photoluminescence emission spectra (λ_{ex} = 350 nm) of the quantum dots in absence and in the presence of increasing quantities of captopril: (a) 0, (b) 8 x 10^{-6}, (c) 1 x 10^{-5}, (d) 2 x 10^{-5}, (e) 3 x 10^{-5}, (f) 4 x 10^{-5}, (g) 5 x 10^{-5}, (h) 7 x 10^{-5} mol L^{-1}

4.3 Optimization of the composition of the 2MPA-CdTe nanoparticle dispersion in buffered media for photoluminescence enhancement

4.3.1 Effect of pH in phosphate buffer solution

The photoluminescence intensity measured from quantum dots dispersions is sensitive to any changes in medium. The acidic nature of captopril can affect the photoluminescence intensity from the photoluminescence probe. Therefore, buffered systems are required in order to access, through the variation of photoluminescence characteristics (photoluminescence enhancement), the effective effect of captopril on quantum dots. As the photoluminescence intensity was significantly dependent upon the variation of the pH of the system, the photoluminescence from the quantum dots were evaluated as they were dispersed in buffered solutions (phosphate buffer 0.01 mol L^{-1}) at the pH range between 6.0 and 9.5. In order to evaluate the effect that captopril causes in the measured signal, the photoluminescence was measured before and after the addition of 1.4 x 10^{-4} mol L^{-1} captopril solution.

In Figure 35, it is indicated the net photoluminescence (ΔF) measured from the quantum dot dispersion at different pH values after the addition of captopril. The ΔF value was the difference between F and $F_{0,}$ where F_0 and F are respectively the photoluminescence of the quantum dots dispersion before and after the addition of 1.4 x 10^{-4} mol L^{-1} captopril. The better photoluminescence enhancement was observed at pH 8.5, therefore, systems containing pH 8.5 phosphate buffers were chosen for all further experiments.

The effect of concentration of phosphate buffer on the measured photoluminescence was investigated in range of 0.5 to 40 mmol L^{-1}. The photoluminescence is highly stable but at higher concentration of buffer (above 10 mmol L^{-1}) the intensity slightly decreased (7 % relative to initial value). The increase of the ionic strength of the solution may affect the electronic properties of the 2MPA-CdTe dispersed in phosphate buffer (Figure 36).

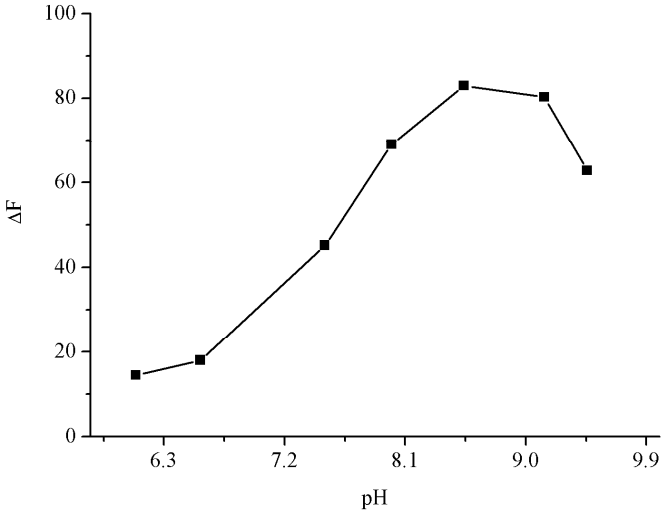

Figure 35 - Effect of pH value (adjusted in phosphate buffer 0.01 molL^{-1}) on the enhancement of the photoluminescence of 2MPA-CdTe quantum dots dispersion (3 x 10^{-8} mol in 1 L of aqueous solution) measured as ΔF = F - F_0 (where F_0 and F are respectively the photoluminescence of the quantum dots dispersion before and after the addition of 1.4 x 10^{-4} mol L^{-1} captopril).

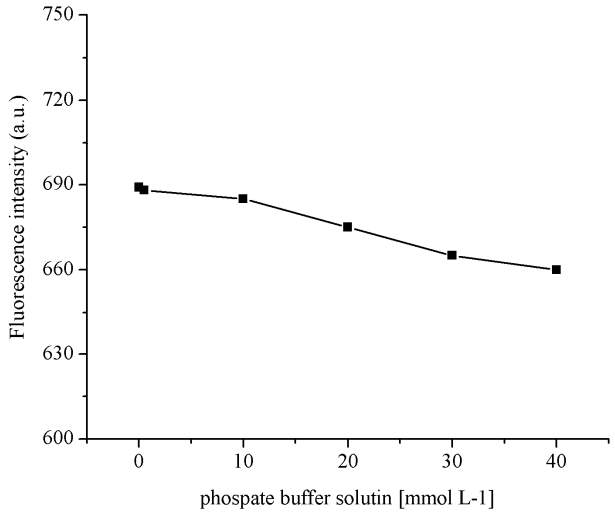

Figure 36 - Effect of different ionic strength of phosphate buffer solution on the photoluminescence of 2MPA-CdTe quantum dots in the presence of 1.4 x 10^{-4} mol L^{-1} of captopril.

4.3.2 Concentration of quantum dots dispersion

The effect of the amount of quantum dots in the buffered system was evaluated. The quantity of the quantum dots was expressed in mol L^{-1} as if it was a real solution. A fixed amount of captopril (1.9×10^{-4} mol L^{-1}) was included in the system in order to make the net photoluminescence measurements (ΔF). The result indicated in Figure 37 shows a large net photoluminescence in the system containing 2.8×10^{-8} mol of nanoparticles in 1 L of aqueous solution. With lower concentrations, the quantity of quantum dots dispersed in the system is too low, which reflected in the small measured photoluminescence. On the other hand, at higher concentrations of quantum dots, the amount of nanocrystals dispersed increases to a large extent and the captopril available to interact with them decreases (molecules available to occupy the number of binding sites required to get an effective interaction), making the net photoluminescence less pronounced. Therefore, the amount of 2.8×10^{-8} mol of the 2MPA-CdTe in 1 L of aqueous solution was chosen to prepare the working dispersion in phosphate buffer solution.

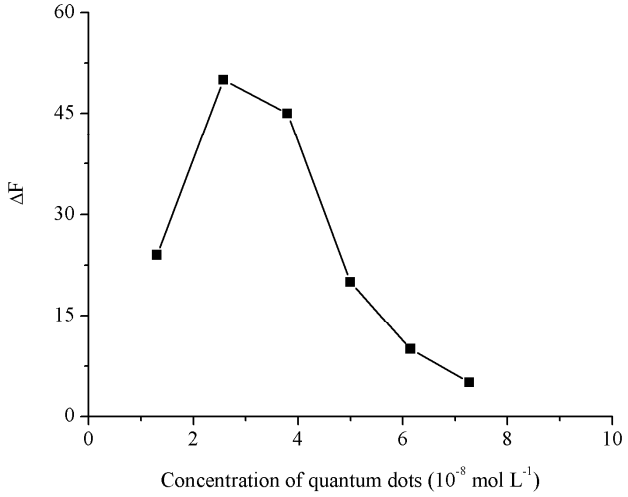

Figure 37 - Effect of concentration of the synthesized quantum dots on the photoluminescence intensity of the aqueous quantum dots dispersion measured as ΔF = F - F_0 (where F_0 and F are respectively the photoluminescence of the quantum dots dispersion before and after the addition of 1.9×10^{-4} mol L^{-1} of captopril.

4.3.3 Photoluminescence stability and reaction time

The variation in photoluminescence intensity measured from the control dispersion of quantum dots in phosphate buffer (0.01 mol L^{-1}) was studied in function of the time (signal measured every 5 min up to 60 min at room-temperature). The result indicated a stable photoluminescence signal proper to analytical purposes (random signal variation of about 2%). The stability of photoluminescence in function of the time, after the mixing a certain amount of captopril (1.4 x 10^{-4} mol L^{-1}) in the quantum dots dispersion, was also evaluated. Photoluminescence was measured every 2 min at room-temperature after the addition and mixing of captopril. The photoluminescence of the 2MPA-CdTe quantum dots rapidly enhanced and the signal kept stable for more than 30 min after the addition of captopril (less than 3% random variation of signal) as indicated in Figure 38. Therefore, in order to obtain reliable quantitative measurements using the quantum dot dispersion, it was established that photoluminescence acquisition must be made after 5 min.

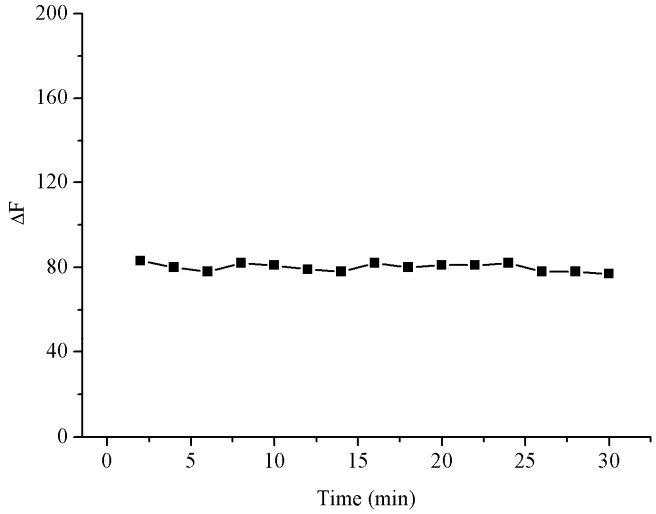

Figure 38 - Photoluminescence stability of 2MPA quantum dots after mixing with 1.4 x 10^{-4} mol L^{-1} of captopril.

4.4 Modeling the interaction of 2MPA-CdTe quantum dots with captopril under optimized condition in aqueous buffered media

To further evaluate the interaction between the 2MPA-CdTe quantum dots and captopril, studies were made in buffered system (phosphate buffer 0.01 mol L^{-1}, pH about 8.5) in order to eliminate the effect of the variation of the pH in the photoluminescence response. Under the optimized conditions (Table 5), the photoluminescence intensity measured from the quantum dots dispersion increased as the concentration of captopril was increased from 5.0 x 10^{-5} to 5.0 x 10^{-4} mol L^{-1} (Figure. 39). The increasing of photoluminescence from the dispersed 2MPA-CdTe nanoparticles in buffered medium behave in an opposite fashion to the signal measured in non-buffered aqueous medium (quenching). However, for concentrations of captopril higher than 5.0 x 10^{-4} mol L^{-1}, no further enhancement of photoluminescence occurs due to the saturation of the surface of the nanocrystals that decreases the availability binding sites (Figure 40).

Table 5- Optimized experimental conditions for the captopril determination using the 2MPA-CdTe probe.

Experimental parameters	Chosen condition
Type of quantum dots	2MPA-CdTe
Phosphate buffer solution	0.01 mol L^{-1}
pH	8.5
Amount of quantum dots	2.8 x 10^{-8} mol per 1 L
Time required to perform measurement	5 min

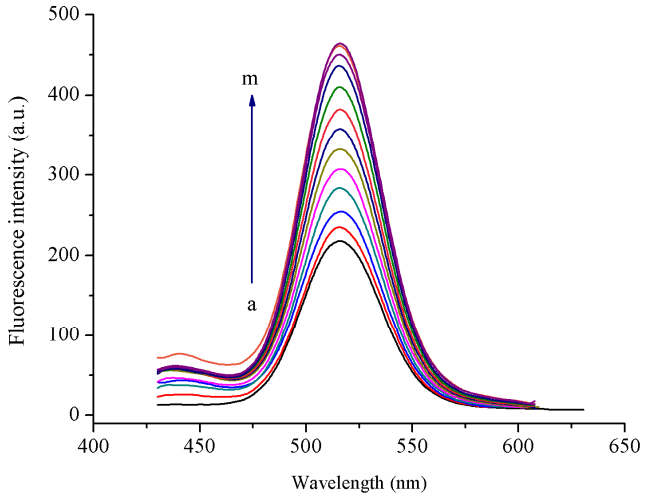

Figure 39 - Photoluminescence emission spectra of CdTe quantum dots in the presence of different concentrations of captopril (mol L^{-1}): pH: 9.0 (a) 0, (b) 9.2 x 10^{-6}, (c) 2x 10^{-5}, (d) 4.6 x 10^{-5}, (e) 9.2 x10^{-5} ^{4}, (f), 1.38x10^{-4}, (g) 1.83 x10^{-4}, (h) 2.71 x10^{-4}, (i) 3.15 x10^{-4} (j) 3.59 x10^{-4}, (k) 4.02 x10^{-4}, (l) 4.44 x10^{-4}, (m) 4.87 x10^{-4}

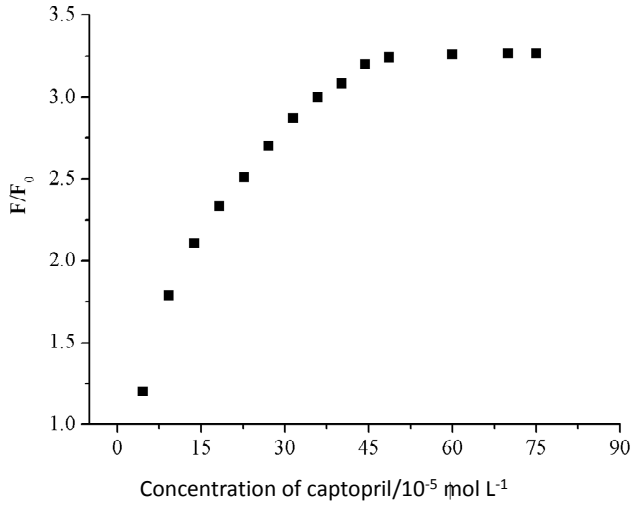

Figure 40 - Non-linear plot of photoluminescence enhancement of 2MPA-CdTe quantum dots in function of the increased concentration of captopril

According to the Langmuir model, if the fraction of occupied sites is defined as θ, the binding rate of captopril will be proportional to the concentration of captopril in solution (C) and the fraction of available binding sites is 1 - θ. The rate of the captopril binding (R_b) to the sites present on the surface of the nanoparticles can be expressed as indicated in Equation 4.1.

$$R_b = K_b\, C\, (1- \theta) \tag{4.1}$$

Where K_b is as binding rate constant. The rate of desorption (R_d) of the bound captopril from the surface is only proportional to fraction of occupied binding sites and can be expressed as indicated in Equation 4.2.

$$R_d = K_d\, \theta \tag{4.2}$$

At equilibrium conditions, the rate of binding can be related to the rate of desorption as indicated in Equation 4.3.

$$K_d\, \theta = K_b\, C(1- \theta) \tag{4.3}$$

The equation can be solved for θ as function of the ratio $B = K_b / K_d$ as indicated in equation 4.4.

$$\theta = (BC\,) / (1+ BC) \tag{4.4}$$

The θ value is related to the ratio between the photoluminescence obtained at a given captopril concentration (F) and the maximum photoluminescence intensity (F_0) that can be achieved, resulting the Equation 4.5.

$$\theta = F / F_0 \tag{4.5}$$

Therefore, an expression that relates the concentration of captopril (C) and the measured photoluminescence intensity can be written as shown in Equation 4.6.

$$F/F_0 = (BC)/(1+ BC) \quad (4.6)$$

This response can be linearized as indicated in Equation 4.7.

$$C/F = (1/BF_0) + (1/F_0)\, C \quad (4.7)$$

4.4.1 Mechanism of interaction

Due to the large surface-to-volume ratio, the exposed surface of the quantum dots is very sensitive to surface changes caused by the interaction with other chemical species. Captopril passivates surface traps on the surface of the semiconductor nanocrystals, minimizing non-radiative de-activation processes. After the addition of captopril in an alkaline solution, the terminal mercapto group of captopril can conjugate to the Cd^{2+} sites present at the surface of the quantum dots, leading to the adsorption-like behaviour modelled by the Langmuir equation. As a result of such binding, the number of surface traps decreases with the consequent increasing of photoluminescence. Works reported in the literature have shown that thiol containing compounds like cysteine passivate quantum dots surface causing the enhancement of the photoluminescence from semiconductor nanocrystals (for instance, the mercaptoacetic acid modified CdSe/ZnS quantum dots) [62].

The absorption spectrum of quantum dots in the presence of captopril is shown in Figure 41. Although there was no shift in the maximum absorption wavelength of 2-MPA-CdTe quantum dots, an increase in the absorbance was observed as the concentration of captopril was increased, which indicates interactions (binding) of captopril (in the ground state) on the surface of the quantum dots.

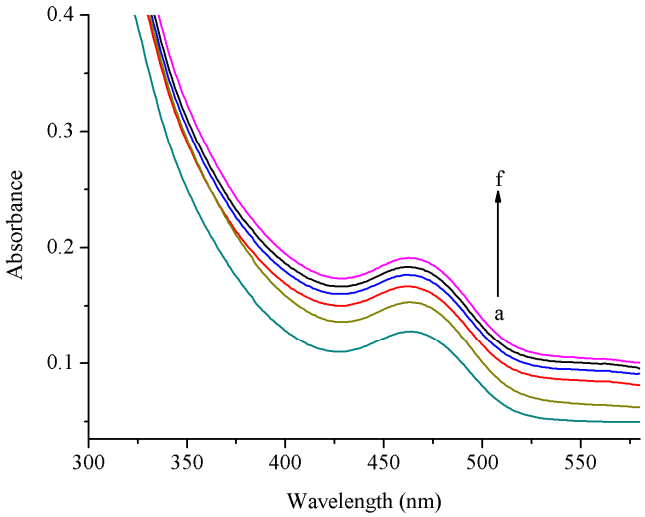

Figure 41 - Electronic absorption spectra of the 2MPA-CdTe quantum dots in the presence of increasing concentrations of captopril: (a) 0, (b) 4.6 x 10^{-5}, (c) 1.4 x 10^{-4}, (d) 2.3 x 10^{-4}, (e) 3.6 x 10^{-4}, (f) 4.9 x 10^{-4} mol L^{-1}.

The interaction between captopril and the quantum dots was further confirmed by Raman spectroscopy (Figure 42), as the spectrum is sensitive to the presence of chemical groups that binds to the surface of the quantum dots. For example, the detection of two overlapped broad Raman bands of 2MPA-CdTe quantum dots between 240 and 360 cm^{-1} has been reported to be a Cd-S bond dependent [162]. In the case of 2MPA-CdTe quantum dots, after the addition of captopril, the appearance of two peaks at 250 and 330 cm^{-1} confirms the binding of captopril to quantum dots surface. As the thiol group of captopril is in a different environment, when compared to the thiol of the ligand 2MPA, the result is a more structured Raman spectrum. Moreover, the appearance of peak at 1360 cm^{-1} after the addition of captopril (corresponding to $-CH_3$ vibration of captopril) confirms the interaction between the analyte and the quantum dots surface.

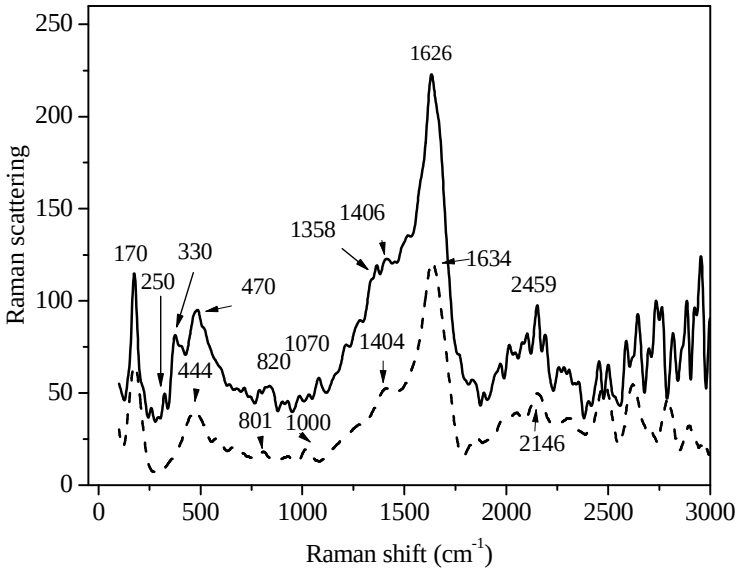

Figure 42 - Raman spectra of 2MPA-CdTe quantum dots disperion before (dashed line) and after the addition of captopril (solid line) .

4.5 Analytical characteristics of enhanced photoluminescence approach

The sensing based on the photoluminescence quenching of quantum dots are usually less selective and sometime the corrections of the inner filter effect caused by the absorbance of light produced by the analyte itself or by sample matrix components are often required in many works. In addition, as the quenching was pH dependent, matrix components would impose severe interferences, impairing the usefulness of such approach. The photoluminescence enhancement approach is favoured in the analytical point of view due to its more selective response that depends upon an effective bindig with the chemical species in solution. Therefore, the photoluminescence enhancement approach was selected for determination of captopril as well as for the interference and stability studies. Signal stability was also an important factor in this choice as it was observed that photoluminescence from control quantum dots dispersed in non-buffered systems decreases in function of time (variations of 18 % after 60 min). On the other hand, the photoluminescence from quantum dots dispersed in bufftered systems is quite stable.

For probing captopril, analytical curves (Langmuir models) were constructed under the optimized experimental conditions by adding increasing concentrations of captopril (C) on the 2MPA-CdTe nanoparticle dispersions. A typical plot of C/F versus C is linear throughout the tested captopril concentration range from 9.2 x 10^{-6} to 4.8 x 10^{-4} mol L^{-1} (final concentration in the working solution) as indicated in Figure 43 [156]. The remarkable Langmuirian fit suggests more than one captopril molecule is binding to the surface of an individual nanoparticle. At higher concentration of captpril no further enhancement of photoluminescence takes place due to decreased availability of binding sites, however at too high concentration, as the pH of nanoparticles dispersion changes, the photoluminescence intensity decrease (quenching).

The regression equation was linear (Y = 0.0018 [captopril] + 2.0 x 10^{-7} with correlation coefficient of 0.9938. The equilibrium binding constant (B) calculated from the ratio of slope/intercept value of the linearized plot (C/F versus C) was 0.082 L mol^{-1}.

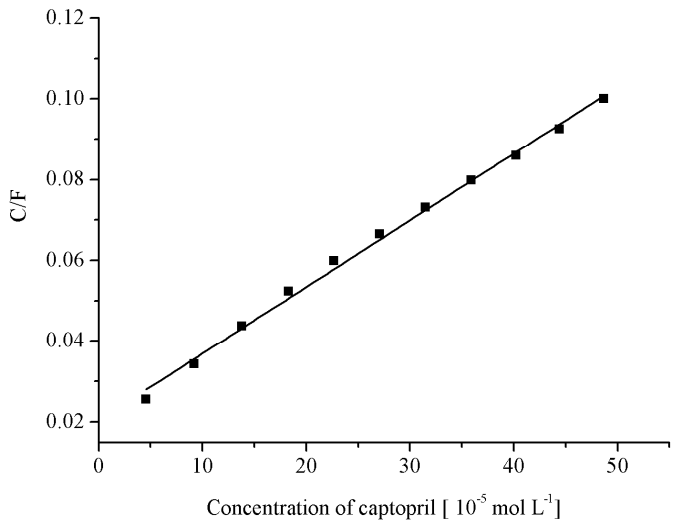

Figura 43 - Langmuir binding isotherm for captopril used to linearize the photoluminescence response in function of the increased concentration of captopril.

The limit of detection (LOD) was calculated as the concentration of captopril that enables a photoluminescence signal equivalent to $F_0 + 3s_{F0}$, where s_{F0} is the standard deviation of ten replicate measurements of the photoluminescence intensity of the working quantum dots dispersion (without captopril). Similarly, the limit of quantification (LOQ) was calculated as the $F_0 + 10s_{F0}$. The LOD and the LOQ were respectively 6.2 x 10^{-6} mol L^{-1} (1.3 μg mL^{-1}) and 7.3 x 10^{-6} mol L^{-1} (1.6 μg mL^{-1}). Precision was calculated based on the propagated standard deviation of C/F (the $s_{C/F}$ value). In order to facilitate calculations, the standard deviations of the parameters of the calibration curve were used to estimate $s_{1/BFo}$ as s_b (the standard deviation of the linear coefficient) and $s_{1/Fo}$ as s_m (the standard deviation of the curve sensitivity) since the relationship in Equation 4.8 may be viewed as the one in Equation 4.9.

$$\frac{C}{F} = \left(\frac{1}{BF_0}\right) + \left(\frac{1}{BF_0}\right) C \tag{4.8}$$

$$\frac{C}{F} = b + mC \tag{4.9}$$

The combined standard deviation of mC (s_{mC}) was calculated as Equation 4.10.

$$s_{mc} = \sqrt{\left(\frac{s_m}{m}\right)^2 + \left(\frac{s_c}{C}\right)^2} \tag{4.10}$$

Where s_{c1} is indicated in Equation 4.11 as the 1 x 10^{-2} mol L^{-1} was directly prepared by the dissolution of the mass of analyte (measured in the balance) and transfering it directly into the volumetric flask of volume V_f that ha a uncertainty of volume of s_{Vf}.

$$s_{c_1} = \sqrt{\left(\frac{s_{balance}}{mass}\right)^2 + \left(\frac{s_{Vf}}{V_f}\right)^2} \tag{4.11}$$

For further dilution a final concentration c_2 is achieved with sc_2 calculated as indicated in Equation 4.12.

$$s_{c_2} = C_2\sqrt{\left(\frac{s_{c_1}}{C_1}\right)^2 + \left(\frac{s_{V1}}{V_1}\right)^2 + \left(\frac{s_{V2}}{V_2}\right)^2} \tag{4.12}$$

In Equation 4.12, s_{v1} is the standard deviation of the micropipette and volume and s_{v2} is the standard deviation of final solution with volume v_2 adjusted in the volumeic flak. The $s_{C/F}$ value is then calculated as indicated in Equation 4.13.

$$s_{\frac{C}{F}} = \frac{C}{F}\sqrt{\left(\frac{s_b}{b}\right)^2 + \left(\frac{s_{mc}}{C_m}\right)^2} \tag{4.13}$$

The values of s_b and s_m were obtained respectively from Equations 4.14 and 4.15.

$$s_b = \sqrt{\left(s^2.\sum X^2\right) - \left(\sum X^2\right)} \tag{4.14}$$

and

$$s_m = \sqrt{\frac{ns^2}{D}} \tag{4.15}$$

D is the deviation of the curve and given by Equation 4.16 .

$$D = \left(n.\sum X^2\right) - \left(\sum X\right)^2 \tag{4.16}$$

Where X is the captopril concentration in the analytical solutions. Combinated standard deviation calculations indicated that the sC/F value, in percent value, is 5.6 % for 1 x 10^{-4} mol L^{-1} of captopril.

4.6 Effect of coexisting substances

The effect of different substances on the photoluminescence signal of the quantum dot working dispersion was evaluated in order to access the selectivity of the interaction between captopril and the 2MPA-CdTe nanocrystals. The chosen substances were the ones commonly found in captopril pharmaceutical formulations (including hydrochorothiazide, a common diuretic administrated together with captopril) and in biological fluids (including several amino acids). As it can be seen in Table 6, the tested substances did not impose significant signal variations (under the 4% tolerance limit established in this work) at the specified tested maximum concentrations. Therefore, these substances at these concentration levels indicate may not interfere during the probing of captopril.

Table 6 - Effect of co-existing substances on the photoluminescence of 2MPA-CdTe quantum dots aqueous dispersion.

Coexisting substances	Concentration (10^{-5} mol L^{-1})	Photoluminescence variation (%)
Cysteine	20	+ 4.0
Histidine	50	+3.1
Tyrosine	50	+1.0
Phenylalanine	50	+2.0
Lactose	500	-2.0
Silicon ioxide	500	+1.5
Hydrochloro-thiazide	1000	-3.0
Citric acid	100	- 0.1
Ascorbic acid	100	- 0.5
SDS	100	-1.3
β- cyclodextrin	100	+1.9

4.7 Application of 2MPA-CdTe quantum dots dispersions in the determination of captopril.

The 2MPA-CdTe aqueous dispersion was tested as probe for the determination of captopril in two different commercials formulations that contained captopril as the only active principle and also in human blood serum. The results obtained for captopril tablets (25 mg per tablet) were satisfactory and in close agreement with the labelled value indicated in the pharmaceutical formulaton instructions (Table 7). These results also indicate that commonly excipients present in tablets did not interfere in the determination. Thus the proposed probe is potentially suitable for analysis of captopril in pharmaceutical formulations.

Table 7- Results of analysis of pharmaceutical tablets containing captopril using the method based on the proposed photoluminescent probe and using an established analytical method (n=3).

Sample	Labeled value mg/tablet	Proposed method mg/tablet	Recovery (%)
A[1]	25	24.6	98.4 ± 1.7
B[2]	25	25.2	100.6 ± 1.2

.Marketed under the trade name of Captopril: A[1] is the Eurofarma Laboratórios Ltda- Brasil and B[2] is the EMS indústria Farmacêutica Brasil

The quantum dots system was also applied for determination of captopril in human blood serum spiked at two concentration levels (6.1×10^{-5} mol L^{-1} and 1.4×10^{-4} mol L^{-1}). The concentration of captopril was calculated by the linearized Langmuir model and the recoveries of captopril in the serum were 97.7 ± 3.8 and 98.8 ± 4.2, respectively, for concentration of 6.1×10^{-5} mol L^{-1} and 1.4×10^{-4} mol L^{-1}. The results obtained in human blood serum were compared with the results achieved a reference method using the Ellman's reagent and spectophotometric determination.

The recovery results of captopril achieved by both methods were in closed agreement as indicated by Student't-test (t_{calc} = 0.84 for 6.1×10^{-5} mol L^{-1} and 1.47 for 1.4×10^{-4} mol L^{-1} with $t_{critical}$ = 2.77 at 95% confidence level and n = 5)

Table 8-Recovery of captopril in human serum with proposed method and by a reference method (n = 5).

Spiked Sample	Expected concentration of captopril mol L^{-1}	Recoveries (%) by the proposed method	Recoveries (%) by the by the reference method [1]
Human serum 1	6.1×10^{-5}	99.6 ± 5.0	97.7 ± 3.8
Human serum 2	1.4×10^{-4}	97.4 ± 3.9	98.8 ± 4.2

[1]The Ellman´s method.