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ORIGINAL PAPER

A Validated Spectrofluorimetric Method for the Determination of Citalopram in Bulk and Pharmaceutical Preparations Based on the Measurement of the Silver Nanoparticles-Enhanced Fluorescence of Citalopram/Terbium Complexes

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Abstract A simple, sensitive, and accurate spectrofluorimetric method was developed for the determination of citalopram in bulk and pharmaceutical preparations. The method is based on the enhancement of the weak fluorescence signal (FL) of the Tb (III)-citalopram system in the presence of silver nanoparticles. Fluorescence intensities were measured at 555 nm after excitation at 281 nm. Prepared silver nanoparticles (AgNPs) were characterized by UV-Visible spectra and transmission electron microscopy (TEM). Various factors affecting the formation of citalopram-Tb (III)-AgNPs complexes were studied and optimized. The fluorescence intensity versus concentration plot was linear over the range 0.02–14 μg mL^{-1}, with an excellent correlation coefficient of 0.9978. The limit of detection (LOD) and limit of quantification (LOQ) were found to be 7.15×10^{-6} μgmL^{-1} and 2.38×10^{-5} μgmL^{-1} respectively. The proposed method was found to have good reproducibility with a relative standard deviation of 3.66 % (n=6). The interference effects of common excipients found in pharmaceutical preparations were studied. The developed method was validated statistically by performing recoveries studies and successfully applied for the assay of citalopram in bulk powder and pharmaceutical preparations. Percent recoveries were found to range from 98.98 % to 100.97 % for bulk powder and from 96.57 % to 101.77 % for pharmaceutical preparations.

Keywords Fluorescence · Citalopram · Colloidal silver nanoparticles · Terbium

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Introduction

Depression is a major issue in today's society because of the inherent personal, social, and economic issues, and the treatment of depression usually involves the administration of medications. Tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) are commonly used in psychiatry for the treatment of major depression. The SSRIs are a recently introduced group of antidepressants and differ from the TCAs in terms of chemical structure and mode of action. The SSRIs are similar to the TCAs in terms of clinical ability but have more favorable pharmacological profiles. Furthermore, they are considered safe and well-tolerated [1, 2].

Citalopram, (CIT) 1-(3-dimethylaminopropyl)-1-(4-fluorophenyl)-1, 3-dihydroisobezofuran-5-carbonitrile [3], is a second generation antidepressant and one of the recently introduced SSRIs. It is used for managing depression, social

anxiety disorder, panic disorder, and obsessive-compulsive disorder [4–6]. Like TCAs, citalopram does not have any known adverse anticholinergic or cardiovascular effects, and is considered safe for the treatment of depression even in children and adolescents [7]. Citalopram is efficiently absorbed in the gastrointestinal tract, and its recommended daily dosage ranges from 20 to 40 mg, which corresponds to plasma drug concentrations of between 30 and 130 $ng mL^{-1}$ [8]. Maximum plasma levels are reached 4 h after oral administration and its plasma half-life is 37 h. Kinetic studies of citalopram have shown rapid almost complete absorption followed by slow elimination [9, 10]. Citalopram is mainly metabolized in the liver by cytochrome P where it undergoes several consecutive N-demethylation steps to produce desmethylcitalopram and didemethylcitalopram. N-oxidation and deamination of citalopram, which lead to citalopram N-oxide and citalopram propionic acid metabolites, respectively, have also been observed [11, 12]. Citalopram is sold as a racemic mixture, consisting of 50 % *R*-(−)-citalopram and 50 %*S*-(+)-citalopram. The *S*-(+)-enantiomer has the desired antidepressant effect [13], and is now available commercially under the generic name escitalopram. Furthermore, it has been shown that the *R*-enantiomer present in citalopram counteracts the activity of escitalopram, and that citalopram and escitalopram have different pharmacological and clinical effects [14].

Several methods have been devised for the determination of citalopram in pharmaceutical preparations and biological fluids. These include high performance liquid chromatography (HPLC) with UV detectors [15–17], HPLC with fluorescence detectors [18–20], HLPC/mass spectrometry [21–23], gas chromatography [24, 25], electrophoretic methods [26–28], and spectrophotometric [29–31] methods. However, few spectrofluorimetric [32–34] methods have been reported in the literature, and most reported methods involve multistep procedures, and have poor selectivities and sensitivities and narrow linear ranges. Although, HPLC methods are sensitive but expensive, involve the use of complicated procedures, and are time-consuming. Spectrofluorimetry is considered as one of the most suitable analytical technique for the analysis of pharmaceutical compounds, because of its low cost, simplicity, low detection limits, wide linear dynamic range, and wide availability.

Lanthanides ions play an important role as luminescence probes in bioanalytical applications because of their sensitivities and selectivity's [35]. Lanthanides sensitized luminescence provides large Stokes shifts, narrow emission bands, and long luminescence lifetimes [36]. Furthermore, it is well known that metallic nanostructures can modify the spectral properties of fluorophores [37, 38]. Metal-fluorophore interactions can greatly enhance luminescence intensity [38], whereby fluorescent species are excited with an external light source and this energy is then partially transferred or coupled to surface plasmones in the metallic nanostructure that significantly enhance luminescence intensity due to metal-fluorophore interactions [38, 39].

The present work was undertaken to develop a simple, sensitive, efficient, and economical spectrofluorimetric method for the determination of citalopram in bulk and pharmaceutical preparations. The effect of the interaction between silver nanoparticles and citalopram-terbium complex in solution on fluorescence intensity was examined [40], and a significant enhancement of terbium-sensitized fluorescence signal by citalopram was observed when AgNPs were added. Furthermore, increases in fluorescence intensity were found to be proportional to the amount of citalopram added. Under optimized conditions, fluorescence intensity was found to be linearly dependent on citalopram concentration in the range 0.02–14 $\mu g mL^{-1}$ with a limit of detection of $7.15\times10^{-6}\,\mu g mL^{-1}$.

Experimental

Materials and Reagents

All reagents used were of analytical grade and used without further purification. Doubly deionized water (DI) was used throughout. Terbium nitrate ($Tb(NO_3)_3.5H_2O$), tris (hydroxyl methyl aminomethane), and silver nitrate were obtained from Sigma-Aldrich, and sodiumborohydride ($NaBH_4$) and sodium citrate from Merck (Germany). Standard reference citalopram was provided by Z-Jan's Pharmaceutical Industry (Hayatabad Peshawar, Pakistan). Commercial formulations of citalopram, that is, Lopram, Citalo, and Pramcit (all as 20 mg tablets) were manufactured by Hansel Pharmaceuticals (Lahore, Pakistan), Platinum Pharmaceuticals (Karachi), and Nabiqasim Industries (Karachi), respectively.

Instruments

A F-4500 spectrofluorometer Hitachi (Japan) equipped with 150-W xenon lamp and photomultiplier tube (Model R 928; Hamamatsu, Japan) and a 1×1 cm quartz cell were used to measure fluorescence intensities. The instrument was operated with excitation and emission slit widths of 5 nm. UV-1800 Shimadzu UV–vis spectrophotometer was used to record absorption spectra. A pH meter (Mettler-Toledo MP 220, US) was used to adjust buffer solution pH values.

Preparation of Reagents Solutions

Terbium nitrate (1×10^{-3}M) was prepared by dissolving 0.02175 g of $Tb(NO_3)_3.5H_2O$ in DI water, diluted to 50 mL with the same solvent, and stored in a refrigerator. Tris–HCl buffer solution (0.1 M) was prepared by dissolving 0.605 g of tris (hydroxyl methyl aminomethane) in 50 mL

deionized water and adjusting its pH with 0.1 $molL^{-1}$ HCl. Working solutions were freshly prepared before use from stock solution by appropriate dilution with DI water.

Preparation of Standard Solution

A standard stock solution of citalopram (250 μgmL^{-1}) was prepared by dissolving 0.0125 g of citalopram standard in 2 mL of distilled ethanol with shaking and diluting to 50 mL with DI water. The stock solution was stored at 4 °C, and working solutions of 10 or 5 μgmL^{-1} were prepared daily by dilution with DI water.

Preparation and Characterization of Silver Nanoparticles

Colloidal solutions of silver nanoparticles were prepared as previously described [41]. Briefly, 25 mL of $AgNO_3$ (1×10^{-3} M) was added dropwise to 75 mL of a freshly prepared aqueous solution of $NaBH_4$ (2×10^{-3} M) with vigorous stirring. After 10 min, 5 mL of sodium citrate solution (1 % w/w) was added to stabilize the AgNPs formed. The yellow colloidal solution of Ag NPs was then stirred for another 20 min and aged for 2 days at 4 °C before use. The prepared AgNPs were characterized by UV-visible spectroscopy (Fig. 1a) and transmission electron microscopy (TEM) (Fig. 1b) (Hitachi-7100, Japan) at an accelerating voltage of 100 kV. TEM images of AgNPs (Fig. 1b) showed that the average diameters of the particles produced was 17±2 nm. Fig. 1(a) shows the UV-visible spectrum of AgNPs and the intense absorption peak at ~396 nm, which is the characteristic plasmonic band of Ag NPs. The concentration of the as-prepared AgNPs was $2.4\times10^{-4}molL^{-1}$, based on the concentration of $AgNO_3$ solution used for their preparation.

Analytical Procedure for Preparation of a Calibration Curve

An appropriate volume of citalopram stock solution, diluted to give a final concentration of 0.02–14 μgmL^{-1}, was added to 10 mL volumetric flasks. Tris–HCl buffer solution (0.5 mL; pH=8), 1.0 mL of $2\times10^{-4}molL^{-1}$ Tb (III) ion solution, and 1.0 mL of $1.4\times10^{-4}molL^{-1}$ Ag NP solution were then added. Mixtures were then diluted to 10 mL with DI water, mixed thoroughly, and allowed to stand for 10 min to allow complex formation. Mixtures were then placed in 1×1 cm quartz cells and fluorescence intensities were measured against a reagent blank at 555 nm after excitation at 281 nm. The voltage for the photomultiplier tube was set at 950 V.

Application to Pharmaceutical Preparations

Five tablets containing nominally 20 mg of active ingredient of citalopram were weighed, and ground to fine powders in a mortar. Powder equivalent to 0.0125 g of citalopram were then dissolved in 2 mL of ethanol, DI water was added, and the mixtures sonicated for 10 min. The resultant solutions were then filtered and diluted to 50 mL with DI water. Appropriate volumes of these solutions were then diluted with DI water such that concentrations of citalopram in final sample solutions were within the working range. Aliquots of these solutions were then analyzed using the procedure described above and actual citalopram contents of tablets were calculated using the calibration equation ($Y = 320X + 0.333$).

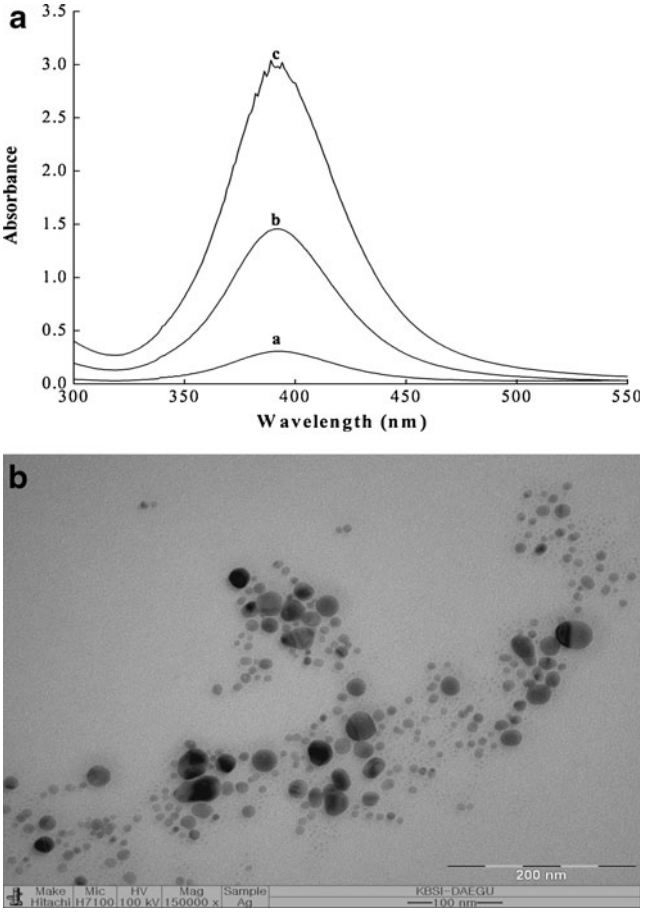

Fig. 1 **a** UV-visible spectrum of the prepared Ag NPs. Conditions; Ag NPs: $2.4\times10^{-5}molL^{-1}$ (*a*); $1.2\times10^{-4}molL^{-1}$ (*b*); $2.4\times10^{-4}molL^{-1}$ (*c*). **b** TEM image of the prepared Ag NPs

Results and Discussion

Spectral Characteristics

The transfer of intermolecular energy from Tb (III) to a ligand is a well-known phenomenon [42, 43]. As shown in Fig. 2a′, the Tb (III) ion has a very weak emission spectrum, but in the presence of citalopram this fluorescence intensity is increased (Fig. 2d′) which shows that

a complex of Tb (III) and citalopram has been formed and intramolecular energy transfer has occurred. Intramolecular energy transfer from citalopram to Tb (III) may enhance the weak luminescence of Tb (III) (Fig. 2d′) that originates from the intra-chelate energy transfer from the triplet state of the organic ligand (CIT) to the excited energy levels of the Tb (III) ion [44]. Because the coordination number of Tb (III) is generally eight [44], it is probably that there are unfilled sites in Tb (III). Since CIT exists in an ionic form in aqueous solution, it can easily interact with Tb (III), and because of the effect of packing in a ternary complex, energy transfer is facilitated, non-radiative energy loss is reduced, and the fluorescence intensity of Tb (III) is increased. Furthermore, the addition of colloidal AgNPs to the CIT-Tb (III) system greatly enhances fluorescence intensities (Fig. 2e′).

Optimization of Reaction Conditions

Effect of pH and Buffer Solutions

The fluorescence intensity of CIT-Tb (III)-Ag NPs system is highly pH dependent. To find the optimum pH of sample solutions for the determination of citalopram, the effect of pH on fluorescence intensities was investigated in the range from 7–10. The results obtained showed that maximum fluorescence intensity was observed at pH 8 (Fig. 3), after which intensity decreased possibly because of the precipitation of terbium hydroxide. The effects of carbonate, borate, phosphate, and Tris–HCl buffer solutions of the same pH were also studied. The maximum fluorescence intensity was observed for the Tris–HCl buffer solution. The effect of buffer volume was also investigated, we found that 0.5 mL of pH 8 Tris–HCl buffer produced maximum fluorescence intensities.

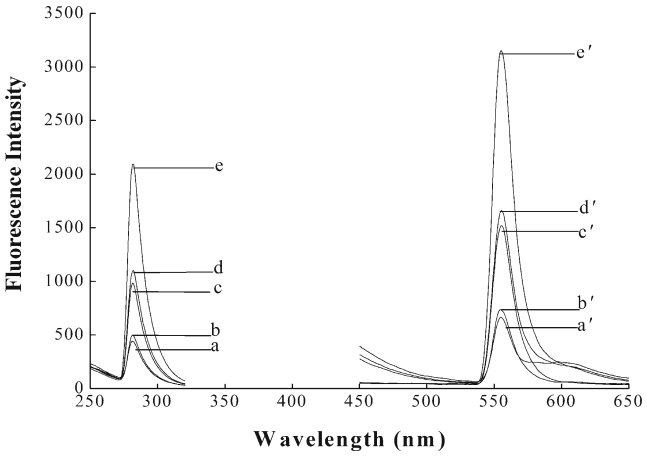

Fig. 2 Excitation and emission spectra of Tb (III) (*a*, *a′*); Citalopram-Ag NPs (*b*, *b′*); Tb (III)-Ag NPs (*c*, *c′*); Tb (III)-citalopram (*d*, *d′*); Tb (III)-citalopram-Ag NPs (*e*, *e′*). Conditions: 14 μg mL^{-1} citalopram; 1.0 mL of 2×10^{-4} mol L^{-1} Tb (III); 0.5 mL of Tris–HCl of pH 8.0; 1 mL of 1.4×10^{-4} mol L^{-1} Ag NPs, diluted to 10 mL

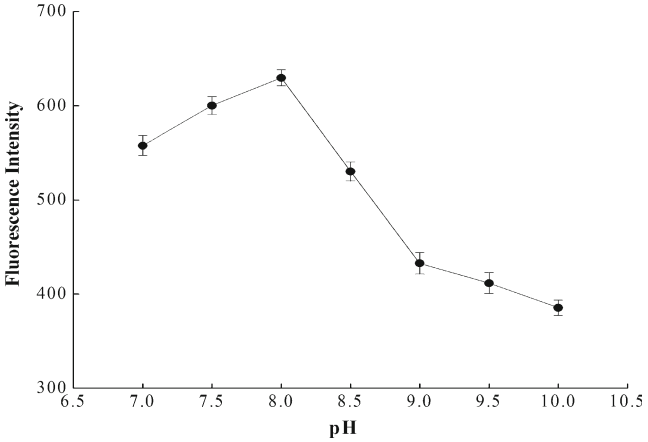

Fig. 3 Effect of pH on fluorescence intensity. Conditions: 14 μg mL^{-1} citalopram; 1.0 mL of 5×10^{-4} mol L^{-1} Tb (III); 1 mL of Tris–HCl of pH (7–10); 1 mL of 1.2×10^{-4} mol L^{-1} Ag NPs, diluted to 10 mL

Effect of Tb (III) Concentration

The effects of Tb(III) concentration on CIT-Tb(III)-AgNP fluorescence intensities were investigated in the range 1–8×10^{-4} mol L^{-1}. Peaked fluorescence intensity was observed at 2×10^{-4} mol L^{-1} of Tb (III) (Fig. 4). The volume of Tb (III) was also optimized and 1 mL of 2×10^{-4} mol L^{-1} Tb (III) produced maximum fluorescence intensity.

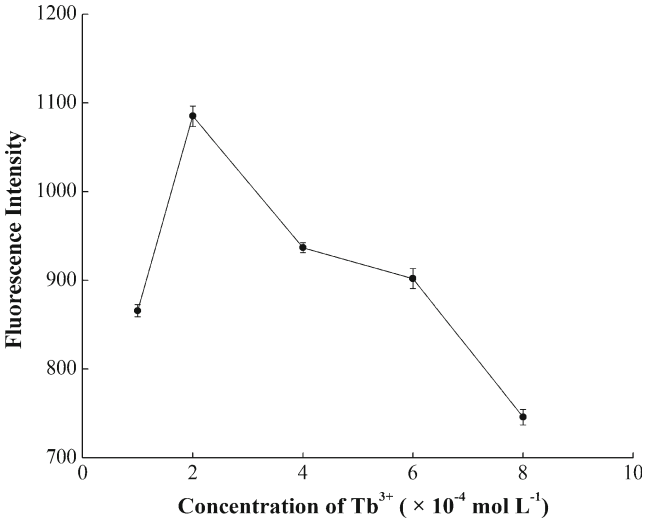

Fig. 4 Effect of concentration of Tb (III) on fluorescence intensity. Conditions: 14 μg mL^{-1} citalopram; 1.0 mL of 1–8×10^{-4} mol L^{-1} Tb (III); 0.5 mL of Tris–HCl of pH 8; 1 mL of 1.2×10^{-4} mol L^{-1} Ag NPs, diluted to 10 mL

Effect of Ag NPs Concentration

The effect of AgNP concentration was studied in the range 6×10^{-5} to 2.2×10^{-4} molL^{-1}. CIT-Tb(III)-AgNP fluorescence intensities increased up to Ag NP concentration of 1.4×10^{-4} molL^{-1} and then decreased (Fig. 5). The effect of Ag NP solution volume was also studied and it was found that 1 mL of 1.4×10^{-4} molL^{-1} Ag NPs produced the maximum signal, and thus, this concentration was used for further analyses.

Fluorescence Stability

Fluorescence stability was investigated by monitoring fluorescent intensity regularly for up to 130 min. No significant change in fluorescence intensity of the CIT-Tb(III)-AgNP system was observed.

Analytical Figures of Merit

The fluorescence intensity of the CIT-Tb(III)-Ag NPs system increases linearly with citalopram concentration. Under optimum experimental conditions, the calibration graph of fluorescence intensity versus citalopram concentration was linear in the range 0.02–14 μgmL^{-1}, with an excellent correlation coefficient of 0.997–0.9993 (Fig. 6a, b). Limit of detection (LOD), as defined by IUPAC, is given by $C_{LOD}=3\ S_b/m$, where S_b is the standard deviation of the blank signals and 'm' is the slope of the calibration graph. In this study, the LOD was found to be 7.15×10^{-6} μgmL^{-1}. On the other hand, limit of quantification (LOQ) is defined by IUPAC as $C_{LOQ}=10\ S_b/m$, and was found to be 2.38×10^{-5} μgmL^{-1}. The linear regression equation, slope, intercept, correlation coefficient, and relative standard deviation of the response factor are given in Table 1. The sensitivity of the proposed method is compared with other reported methods in Table 2, which shows that sensitivity of the present method is greater than those of previously reported methods.

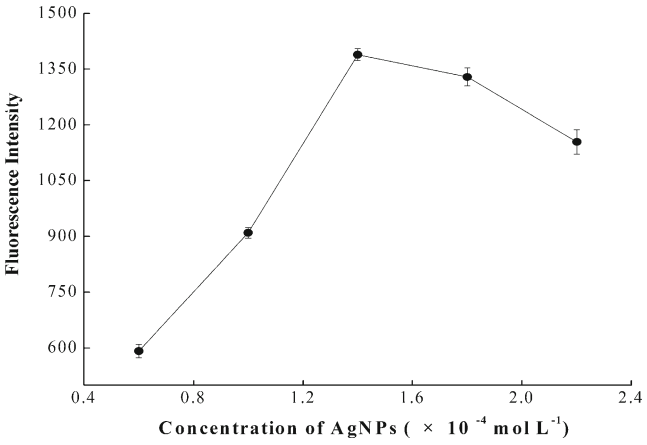

Fig. 5 Effect of concentration of Ag NPs on fluorescence intensity. Conditions: 14 μgmL^{-1} citalopram; 1.0 mL of 2×10^{-4} molL^{-1} Tb (III); 0.5 mL of Tris–HCl of pH 8; 1 mL of 0.6–2.2×10^{-4} molL^{-1} Ag NPs, diluted to 10 mL

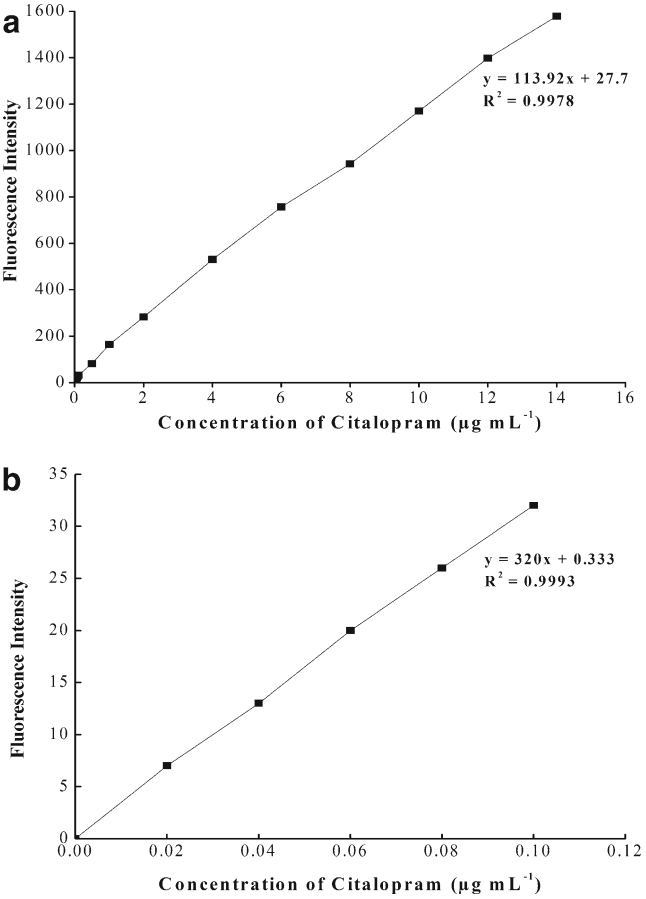

Fig. 6 **a** Linear range of citalopram. Conditions: 0.02–14 μgmL^{-1} citalopram; 1.0 mL of 2×10^{-4} molL^{-1} Tb (III); 0.5 mL of Tris–HCl of pH 8; 1 mL of 1.4×10^{-4} molL^{-1} Ag NPs, **b** Calibration curve of citalopram. Conditions: 0.02–0.1 μgmL^{-1} citalopram; 1.0 mL of 2×10^{-4} molL^{-1} Tb (III); 0.5 mL of Tris–HCl of pH 8; 1 mL of 1.4×10^{-4} molL^{-1} Ag NPs

Table 1 Analytical parameters of the spectrofluorimetric determination of citalopram

Parameter	Value
λ_{exc} (nm)	281
λ_{eme} (nm)	555
Linear range (μgmL^{-1})	0.02–14
Limit of detection (μgmL^{-1})	7.15×10^{-6}
Limit of quantification (μgmL^{-1})	2.38×10^{-5}
Regression equation (y)	$Y = 320X + 0.333$
Slope (b)	320
Intercept (a)	0.333
Correlation coefficient (r)	0.9993
Standard deviation (μgmL^{-1})	7.630×10^{-4}
Relative standard deviation (%)	3.66

Table 2 Comparison of the present method and other reported methods for the determination of citalopram levels

Methods	Linear range	Limit of detection (LOD)	References
HPLC	20–80 $\mu g L^{-1}$	5 $\mu g L^{-1}$	[23]
Capillary Zone Electrophoretic	1–20 $mg L^{-1}$	0.03 $mg L^{-1}$	[26]
Spectrophotometry	10–250 $\mu g mL^{-1}$	5.2 $\mu g mL^{-1}$	[29]
Spectrophotometry	8–240 $\mu g mL^{-1}$	4.14 $\mu g mL^{-1}$	[30]
Spectrofluorimety	5.0×10^{-7}–2.5×10^{-6}M	8.0×10^{-6}M	[33]
Spectrofluorimety	0.06–0.64, 0.04–0.40, 0.02–0.26 ($\mu g mL^{-1}$)	0.02, 0.01,0.007 ($\mu g mL^{-1}$)	[34]
Spectrofluorimetry	0.02–14 $\mu g mL^{-1}$	$7.15\times10^{-6}\mu g mL^{-1}$	Present method

Interferences Study

In real samples, interferents may be present that could suppress or enhance the fluorescence signal of the analyte under investigation. Therefore, the effects of glucose, fructose, starch, lactose, talc, and magnesium stearate, which are commonly used in pharmaceutical tablets were studied (Fig. 7). The interference study was carried out by preparing samples containing a fixed amount of citalopram (0.02 μg mL^{-1}) and 5, 10, and 20 fold concentrations ladders of excipients. A 5 % error criterion was adopted. None of these common excipients was found to cause interference. Average recoveries obtained were in the range 97.77 %–101.34 % (Table 3).

Reliability of the Method

The precision of the developed method was studied by determining citalopram in pure form and pharmaceuticals

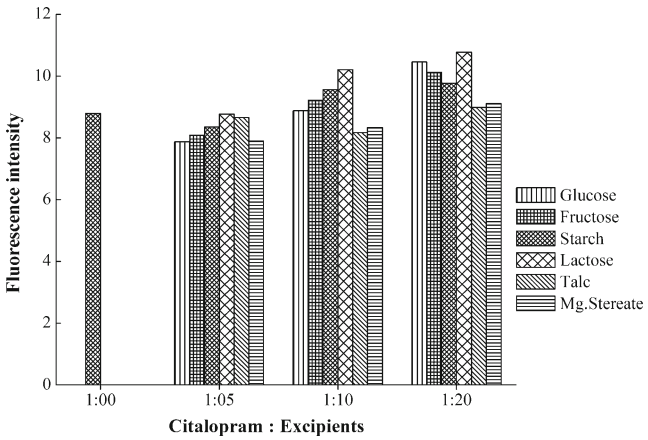

Fig. 7 Effect of excipients on fluorescence intensity

Table 3 Percent recoveries of citalopram (0.02 $\mu g mL^{-1}$) in the presence of excipients

Excipients	Excipients added ($\mu g mL^{-1}$)	Drug : Excipients	% Recovery ± RSD
Glucose	0.1	1:05	98.87±2.23
	0.2	1:10	99.12±1.65
	0.4	1:20	98.45±2.22
Fructose	0.1	1:05	99.21±3.31
	0.2	1:10	97.77±3.08
	0.4	1:20	98.22±4.21
Starch	0.1	1:05	100.12±1.23
	0.2	1:10	100.56±3.21
	0.4	1:20	101.34±2.78
Lactose	0.1	1:05	98.88±4.31
	0.2	1:10	99.94±2.11
	0.4	1:20	97.97±1.73
Talc	0.1	1:05	100.32±3.21
	0.2	1:10	99.56±4.11
	0.4	1:20	98.65±2.35
Magnesium. Stearate	0.1	1:05	99.16±1.56
	0.2	1:10	100.54±2.81
	0.4	1:20	98.55±3.32

Results are the averages of three separate analyses; *RSD* Relative standard deviation

preparations using three different concentrations within the calibration curve range, in triplicate. Results are listed in Table 4 for the standard and in Table 5 for pharmaceutical preparations. The percent recoveries obtained ranged from 98.98 % to 100.97 % for the standard and 96.29 % to 102.14 % for pharmaceutical preparations with narrow relative standard deviations, indicating that proposed method has good reproducibility. The accuracy of the present method was investigated by standard addition method using three different brands of tablets Pramcit, Lopram, and Citalo (all contain 20 mg of citalopram). Certain amounts of standard citalopram solution were added to tablet solutions and

Table 4 Accuracy and precision of the present method using standard citalopram

Amount taken ($\mu g mL^{-1}$)	Amount found ($\mu g mL^{-1}$)	% Recovery±RSD
0.02	0.0197	98.98±1.40
0.04	0.0403	100.97±2.38
0.06	0.0605	100.97±1.63
Mean		100.30
± SD		1.148
t-test		0.452 (4.303)

Results are the averages of three separate analyses; *RSD* Relative standard deviation

Table 5 Evaluation of accuracy and precision of the present method for citalopram determination in pharmaceutical preparations

Pharmaceutical preparations	Amount taken ($\mu g mL^{-1}$)	Amount found ($\mu g mL^{-1}$)	% Recovery± RSD
Pramcit, 20 mg tablet	0.02	0.0204	102.14±4.29
	0.04	0.0403	100.91±2.81
	0.06	0.0598	99.72±3.22
Lopram, 20 mg tablet	0.02	0.0201	100.80±3.81
	0.04	0.0388	97.09±4.74
	0.06	0.0599	99.86±3.25
Citalo, 20 mg tablet	0.02	0.0203	101.95±4.60
	0.04	0.0385	96.29±4.25
	0.06	0.0602	100.39±2.91

Results are the averages of three separate analyses; *RSD* Relative standard deviation

analyzed as described above. Recoveries were calculated by comparing the results obtained before and after adding standard citalopram solution, and percent recoveries ranged from 96.57 % to 101.77 % (Table 6).

Applicability of the Proposed Method

The devised method was successfully applied to the determination of citalopram in the three pharmaceutical preparations. The results obtained were in close agreement with label quantities (Table 7), which shows that the proposed method can be used to determine citalopram quantities in pharmaceutical formulations.

Possible Mechanism of Fluorescence Enhancement

The possible mechanism of fluorescence enhancement by Ag NPs can be explained as follows. It has been reported

Table 6 Evaluation of citalopram recovery percent in commercial formulations (tablets) using the standard addition method

Pharmaceutical preparations	Amount added ($\mu g mL^{-1}$)	Amount found ($\mu g mL^{-1}$)	% Recovery± RSD
Pramcit, 20 mg tablet	0.01979	0.02015	101.77±5.47
	0.04038	0.04007	99.19±4.55
	0.06058	0.05975	98.63±2.10
Lopram, 20 mg tablet	0.01979	0.01998	100.96±4.22
	0.04038	0.04039	100.02±3.25
	0.06058	0.06073	100.25±0.65
Citalo, 20 mg tablet	0.01979	0.01996	100.85±3.48
	0.04038	0.03900	96.57±2.82
	0.06058	0.05955	98.30±2.59

Results are the averages of three separate analyses; *RSD* Relative standard deviation

Table 7 Determination of citalopram in pharmaceutical preparations (tablets)

Brand name	Active ingredient (mg/tablet)		
	Label value	Found value± SD	% Recovery± RSD
Pramcit, 20 mg tablet	20	20.16±0.235	100.80±1.17
Lopram, 20 mg tablet	20	19.82±0.372	99.12±1.86
Citalo, 20 mg tablet	20	19.87±0.551	99.36±2.75

Results are the averages of three separate analyses; *RSD* Relative standard deviation

that the Ag NPs modify the free space absorption condition of fluorophores, and that this dramatically changes spectra from those obtained in the absence of metallic nano surfaces [45]. The interaction between excited-state fluorophores and the surface plasmon electrons of metal nanoparticles can enhance resonance energy transfer to the fluorophore [46]. Accordingly, we suggest that the Tb(III)-CIT complex may interact with the surface plasmon electrons of Ag NPs and the fluorophore may be in close vicinity with Ag NPs so influenced. Ag NPs with Tb(III)-CIT complex are excited by non-radiative coupling between the excited fluorophore Tb(III) and the surface plasmonic electrons of Ag NPs which is consequently radiated by nanoparticles themselves. Therefore, the absorption of light may be enhanced by the fluorophores due to an increased electric field between and around nanoparticles [47]. It is clear from the excitation spectra (Fig. 2) that the intensity of the excitation spectra of Tb(III)-CIT-Ag NPs is strongly enhanced (Fig. 2e) as compared to that of CIT-Ag NPs complex (Fig. 2b), Tb (III)-Ag NPs complex (Fig. 2c) and Tb(III)-CIT complex (Fig. 2d). This suggests that the AgNPs enhance the luminescence of Tb(III)-CIT complex by increasing local excitation fields around the edges of particles. Thus, when solutions containing Tb(III)-CIT-AgNPs are excited with an external light source, the energy of the electronically excited state is transferred or coupled to the surface plasmones in metallic nanostructures. This could lead to the fluorescence enhancement of the reported FL system.

Conclusion

A fast, simple, and sensitive method was developed for the determination of citalopram using silver nanoparticle-enhanced terbium-sensitized fluorescence. The enhancement of the fluorescence signal of Tb(III)-CIT complex by Ag NPs allowed us to assay citalopram with high sensitivity and selectivity. The developed method was found to have a wider linear range and lower limits of detection and quantification than other reported methods. Furthermore, the

developed method was successfully used to quantify citalopram levels in commercial tablet formulations with good recovery and excellent reproducibility. Finally, excipients commonly found in pharmaceutical preparations did not interfere with the analysis.

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