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pH Assist for Highly selective determination of Xipamide by the enhancement of the green emission of Tb3+ optical sensor

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Abstract

The highly selective, accurate method for determination of Xipamide was maintained. The method depends on the enhancement of the green emission band of Tb^{3+} at 545 nm in the presence of different concentration of Xipamide at pH 4.1 and λ_{ex} = 320 nm in acetonitrile. The photophysical properties of the green emissive Tb^{3+} complex have been elucidated, the terbium was used as optical sensor for the assessment of Xipamide in the pharmaceutical tablets and body fluids with a concentration range 5.0×10^{-9} – 2.3×10^{-6} mol L^{-1} of xipamide, correlation coefficient of 0.995 and detection limit of 8.5×10^{-10} mol L^{-1}.

Keywords: Xipamide; Terbium(III); Enhancing; Luminescence; Optical sensor.

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Introduction

Xipamide, N-(2,6-dimethylphenyl)sulphamido-5-chloro-4-salicylamide Fig. 1. It is a new diuretic drug. Thiazide and thiazide-like diuretics are extremely useful in the treatment of edema associated with heart failure, cirrhosis of the liver or nephritic syndrome. These diuretics are primary agents in the control of hypertension either alone or in combination with other drugs depending on its severity. Generally, thiazide and thiazide-like diuretics decrease blood pressure 10 to 15 mmHg within the first 3 to 4 days of continuous treatment [1]. Several methods have been published for determination of these drugs. These methods include spectrophotometry [2–12], fluorometry [7], chromatography [12–22], electrophoresis [23–29] and electrochemical methods [30–34]. Voltammetric, chromatographic and electrophoretic methods usually used expensive instruments that may not be available in some quality control laboratories. In this work, xipamide (Xip) concentration was determined by the complexation between (Xip) as a ligand and the Tb^{3+} ion and the possibility of the enhancement of the Tb^{3+} luminescence sensitized by (Xip) was established and investigated. The absorption and emission spectra of (Xip) and (Xip–Tb^{3+}) complex were measured in acetonitrile at pH 4.1. This method is simple, accurate and can successfully be applied to the determination of (Xip) in pharmaceutical preparation and in serum samples with remarkably satisfactory results.

2. Experimental

2.1. Materials

Pure standard xipamide supplied by the National organization for Drug control and Research (Giza, Egypt). Pharmaceutical preparation of Epitens® tablets (Egyptian Pharmaceutical Industries Co., [EIPICO] Tenth of Ramadan city, Egypt) labeled to contain 10 mg of xipamide.

2.2. Reagents

All chemicals used are of analytical grade and pure solvents were purchased from (Aldrich). A stock solution of xipamide (Xip) (1.0×10^{-2} mol L^{-1}) was freshly prepared by dissolving 0.093g in 25 mL pure ethanol. More diluted solution (1.0×10^{-4} mol L^{-1}) was prepared by appropriate dilution with acetonitrile. Stock and working solutions are stored at 4ºC when are not in use.

A Tb^{3+} ion stock solution (1.0×10^{-2} mol L^{-1}) was prepared by dissolving 0.0109g $Tb(NO_3)_3.5H_2O$ (delivered from Aldrich- 99.99%) in small amount of ethanol in 25 mL measuring flask, then dilute to the mark with ethanol. The working solution of Tb^{3+} ion of 3×10^{-4} mol L^{-1} was obtained by appropriate dilution with acetonitrile. The pH = 4.1 was adjusted by using 0.1 mol L^{-1} of Acetic acid solution.

2.3. Apparatus

All fluorescence measurements are carried out on Perkin Elmer LS 45 spectrofluorophotometer in the range (290 – 750 nm with attenuator 30%). The absorption spectra are recorded with Thremo UV-Visible double-beam spectrophotometer. All pH measurements are made with a pHs-JAN-WAY 3040 ion analyzer.

2.4. General procedure

To 10 mL measuring flasks, solutions were added in the following order: 0.1 mL of $1x10^{-2}$ mol L^{-1} XIP solution and 0.3 mL of $1x10^{-2}$ mol L^{-1} Tb^{3+} solution to give $1x10^{-4}$ mol L^{-1} of XIP and $3x10^{-4}$ mol L^{-1} of Tb^{3+}. The mixture was diluted to the mark with acetonitrile and pH was adjusted at 4.1 by using 0.1mol L^{-1} of Acetic acid solution. The above procedure was used for the subsequent measurements of absorption, emission spectra and effect of pH and solvents. The luminescence intensity was measured at $\lambda_{ex}/\lambda_{em}$ =320/545nm.

2.5. Determination of xipamide in pharmaceutical preparations

Five tablets of Epitens® were carefully weighed and ground to finely divided powders. Accurate weights equivalent to 1.5 mg Epitens® was dissolved in 50 mL acetonitrile and mixed well and filtered up using 12 mm filter paper. The concentration of the drug was determined by using different concentrations from the corresponding calibration graph.

2.6. Determination of xipamide in serum solution

3 mL of trichloroacetic acid was added to 1.0 mL serum of a real health volunteer and the solution was centrifuged for 15 min at 4000 r/min to remove proteins, then 100 µL of the serum was added to 0.3 mL of Tb^{3+} stock solution (1×10^{-2} mol L^{-1}) in 10 mL measuring flask and complete to the mark with acetonitrile and the pH was adjusted to 4.1. The luminescence intensity of the test solution was measured before and after addition of Tb^{3+} optical sensor. The change in the luminescence intensity was used for determination of xipamide in serum sample.

2.7. Determination of xipamide in urine solution

Urine sample of healthy people was collected from volunteer who received a single oral dose of 10 mg of Epitens® tablet. The treatment procedure of used urine sample was carried out according to the method described by N.A. Al-Arfaj [35]. 1.0 mL urine sample was pipetted into clean 10 mL centrifugation vial. 0.1 mL of 0.1 mol/L NaOH solution was added, shaken for few seconds, followed by the addition of 5 mL dichloromethane. The mixture was vortex mixed at high speed for 2 min and then centrifuged at 4000 rpm for 10 min. The resulting supernatant was transferred to a

small conical flask. The extract was evaporated to dryness at 60 °C and the residue was dissolved in 0.5 mL water and then analyzed according to the proposed procedure

3. Result and Discussion

3. 1. Absorption and Emission Spectra

The absorption spectra of XIP and Tb^{3+}- XIP complex are shown in Fig. 2. Comparing the spectrum of the XIP with its spectra after the addition of different concentrations of Tb^{3+} ion in acetonitrile, a red shift was observed and the absorbance is also enhanced which indicates that XIP can form a complex with Tb^{3+} ion.

The emission spectra of Tb^{3+}– XIP complex in different concentrations of XIP are shown in Fig. 3. After the addition of different concentrations of XIP into the Tb^{3+} ion in acetonitrile, the intensity of the characteristic peak at 545 nm of Tb^{3+} was enhanced indicating that XIP can form a complex with Tb^{3+} ion. The characteristic peaks of Tb^{3+} ion appear at ($^5D_4 \rightarrow {}^7F_6$ = 490 nm, $^5D_4 \rightarrow {}^7F_5$ = 545 nm, $^5D_4 \rightarrow {}^7F_4$ = 590 nm, $^5D_4 \rightarrow {}^7F_3$= 620 nm and $^5D_4 \rightarrow {}^7F_2$ = 650 nm).

3.2. Effect of experimental variables

3.2.1. Effect of the amount of XIP and Tb^{3+}

The ion titration revealed that the complex formed M : L (3 : 1) for Tb and XIP, which indicates that the metal may coordinate to the ligand from different coordination sites and not only through oxygen of the ketone ring, but the more preferred coordination sites are the O of the ketone group and the nitrogen of the amide ring because they have the highest negative charges, Fig. 4.

3.2.3. Effect of pH

The pH of the medium has a great effect on the luminescence intensity of the Tb-XIP. The pH has been adjusted using Acetic acid solution. The optimum pH value where the peak at 545 nm has the highest intensity was obtained at pH = 4.1, Fig. 5.

3.2.4. Effect of solvent

The influence of the solvent on the luminescence intensities of the solutions containing 1.0×10^{-4} mol L^{-1} of XIP and 3.0×10^{-4} mol L^{-1} Tb^{3+} was studied under the conditions established above. The results show the enhanced emission of Tb^{3+}-XIP in CH_3CN. This can be attributed to the formation of anhydrous solvates of Tb^{3+}-XIP complex introducing solvent molecules in the first coordination sphere of Tb^{3+}-XIP leads to the enhancement of the intensity of all transitions ($^5D_4 \rightarrow {}^7F_6$ = 490 nm, $^5D_4 \rightarrow {}^7F_5$ = 545 nm, $^5D_4 \rightarrow {}^7F_4$ = 590 nm, $^5D_4 \rightarrow {}^7F_3$= 620 nm and $^5D_4 \rightarrow {}^7F_2$ = 650 nm). especially $^5D_4 \rightarrow {}^7F_5$ transition in Tb^{3+}.

3.3. Analytical performance

3.3.1. Method Validation

3.3.1.1. Analytical parameters of optical sensor method

A linear correlation was found between luminescence intensity of XIP– Tb^{3+} complex at λ_{em} = 545 nm and concentration of XIP in the ranges given in Table 1. The calibration curve was obtained by plotting the peak intensity of Tb^{3+} at λ_{em} = 545 nm versus the concentration of XIP and the graph was described by the regression equation:

$$Y = a + bX$$

(Where Y = luminescence intensity of the optical sensor at λ_{em} = 545 nm; a = intercept; b = slope and X = concentration in nmol mL^{-1}). Regression analysis of luminescence intensity data using the method of least squares was made to evaluate the slope (b), intercept (a) and correlation coefficient (r) and the values were presented in Table 1. The limit of detection (LOD) and quantitation (LOQ) calculated according to ICH guidelines [36] using the formulae:

LOD = 3.3 S/b and LOQ = 10 S/b, (where S is the standard deviation of blank luminescence intensity values, and b is the slope of the calibration plot) are also presented in Table 1. The low value of LOD indicates the high sensitivity of the proposed method when compared by other methods [2-34]

3.3.1.2. Application to formulations

The proposed method was applied to the determination of XIP in one representative tablet of Epitens® was purchased from local market and containing other inactive ingredients and in serum sample of the health state human. The results in Table 2 show that the method is successful for the determination of XIP and that the excipients in the dosage forms did not interfere. The results obtained (Table 2) were statistically compared with the official British Pharmacopoeia [B.P] method [37]. The average recovery and R.S.D for the tablet, serum and urine sample in proposed method were (100.2 %, 99.6 and 104.1 %) respectively. Data obtained by B. P method average recovery 99.5%, 99.8 and 98.8 for the tablet, serum and urine samples respectively; and R.S.D was also presented for comparison and shows a good correlation with those obtained by the proposed method. The results obtained by the proposed method agreed well with those of reference method and with the label claim (Table 2).

4. Conclusion

The Tb^{3+} ion in acetonitrile has high sensitive and characteristic peaks in the presence of XIP. The proposed method for the determination of XIP offers simple, rapid and sensitive method for the analysis of XIP in acetonitrile and pH 4.1 with a linear range of $5.0 \times 10^{-9} - 2.3 \times 10^{-6}$ mol L^{-1} and detection limit of 8.5×10^{-10} mol L^{-1}. The developed optical sensor is selective, accurate and attractive for routine control analysis of the drug.

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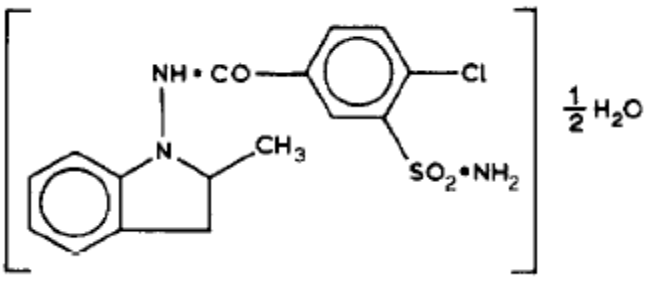

Fig. 1. Chemical structure of xipamide

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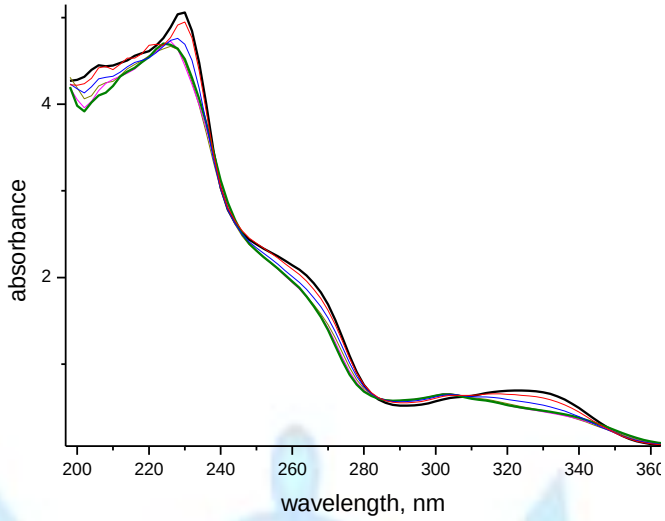

Fig. (2). Absorption spectra of 1x 10^{-4} mol/L xipamide (1) and xipamide in different concentrations of Tb^{3+} ion (2-6).

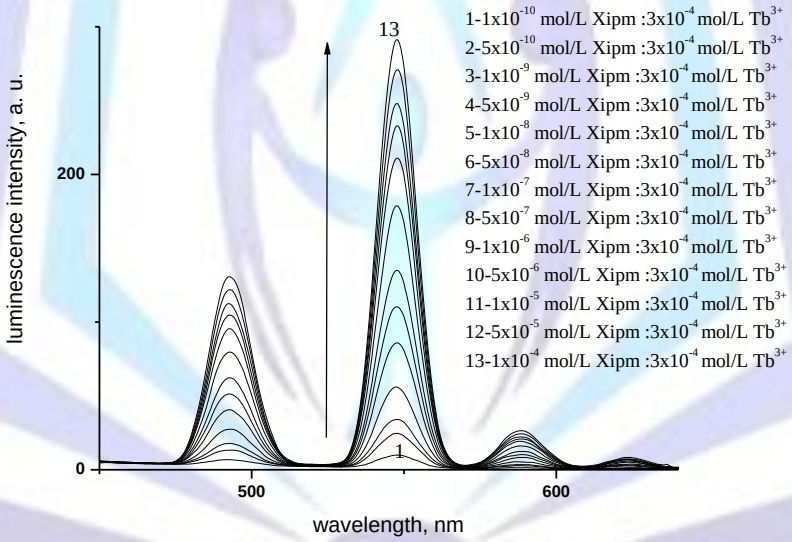

Fig. (3). Luminescence emission spectra of 3x 10^{-4} mol/L Tb^{3+} in different concentrations of xipamide at pH 4.1 and λ_{ex}= 320 nm in acetonitrile.

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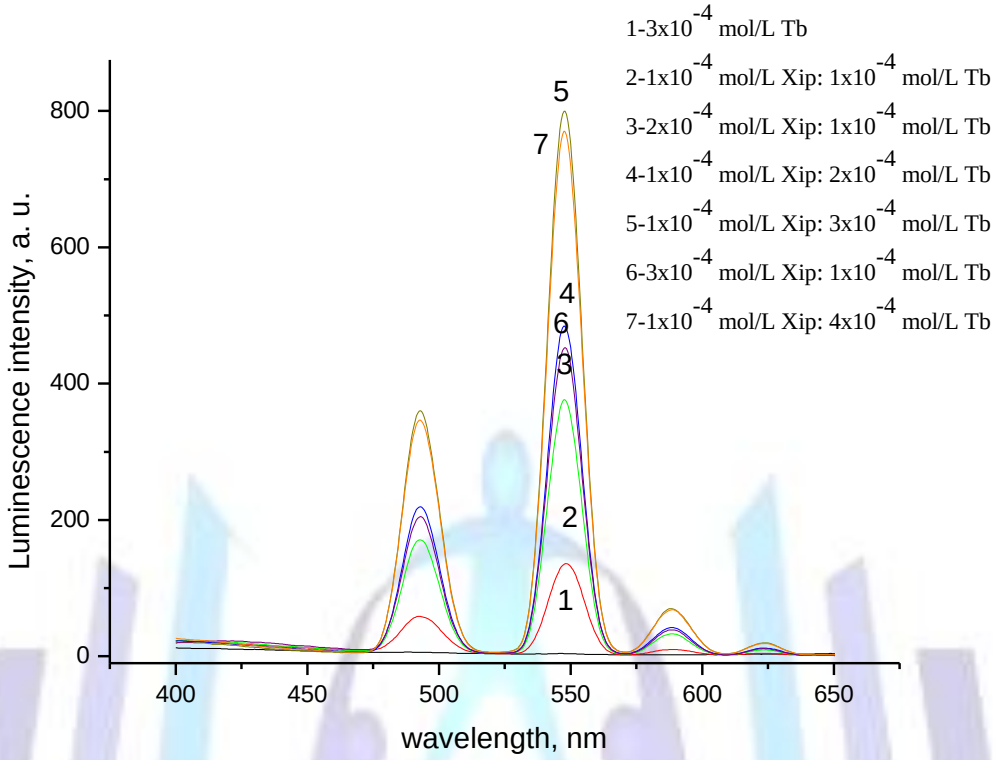

Fig. (4). Luminescence emission spectra of 3x 10^{-4} mol/L Tb^{3+} in different molar ratio of xipamide.

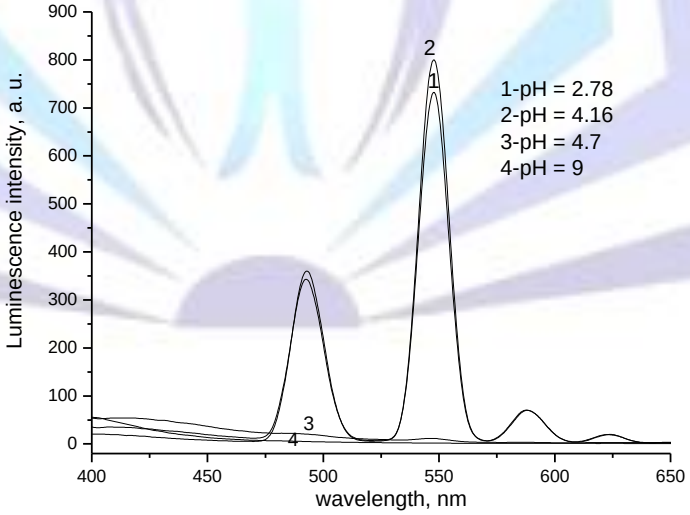

Fig.(5) . Luminescence emission spectra of 3x10^{-4} mol/L Tb^{3+} in the presence of 1x10^{-4} mol/L xipamide in acetonitrile and λ_{ex}= 320 nm in different pH.

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Tables:

Table (1): Sensitivity and regression parameters for the proposed method.

Parameter	
λ_{em} nm	545
Linear range, mol L^{-1}	5×10^{19} - 2.3×10^{-6}
Limit of detection (LOD), mol L^{-1}	8.5×10^{-10}
Limit of quantification (LOQ), mol L^{-1}	2.5×10^{-9}
Intercept a	9.9
Slope b	2.2×10^{8}
Standard deviation	0.07
Variance	0.049
Regression coefficient	0.995

Table 2. Results of recovery study using standard addition method

	Proposed method			
Tablet studied	***Xipamide in Tablet extract x 10^{-7} mol L^{-1}***	***Pure Xipamide added x 10^{-7} mol L^{1}***	***Total Xipamide found x 10^{-7} mol L^{-1}***	***Pure Xipamide recovered (Percent±SD)***
Tablet	10	1.0	10.40	0.48± 99.10
	1.0	4.0	4.95	0. 42 ± 98.75
	0.1	2.5	2.65	0.73 ± 101.09
Urine sample	10	1.0	11.38	0.61 ± 98.96
	1.0	4.0	5.15	0.91 ± 103.75
	0.1	2.5	2.43	0.75 ± 96.3
Serum sample	10	1.5	11.46	1.25± 99.7
	1.0	4.0	4.92	0.25 ± 98.0
	0.1	2.5	2.61	0.85 ± 100.2