شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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جامعة عين شمس

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قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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HANAA ALY

Ain Shams University
Faculty of Science
Chemistry Department

Lanthanide complexes as photo probes for the assessment of some drugs in different body fluids

A Thesis Submitted by

Tarek Ahmed Amin Mohamed Eid
(M. Sc., Analytical Chemistry 2012)

In Partial Fulfillment of the Requirement for the Degree of Doctor Philosophy in science (Chemistry)

Department of Chemistry

Faculty of Science
Ain Shams University

(2021)

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To
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Ain Shams University
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pH assists for selective determination of Acyclovir by the Emission Enhancement of Tb3+Chemosensor in tablet and serum samples

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Abstract

A new selective method for the determination of acyclovir in tablets and serum samples was developed. The method depends on the luminescence enhancement of Tb3+ chemo sensor with different concentrations of acyclovir at pH 10. Acyclovir can form a complex with Tb3+ ion of 1:3 molar ratio in DMSO. The luminescence intensity of Tb3+-acyclovir complex increases as the concentration of the drug increases at λex=320 nm, pH 10 in DMSO. The linear range for determination of the selected drug in DMSO 1.0 x 10-9 –1 x 10-5 mol L-1 the detection limits were 0.24 x 10-9 mol L-1.

Keywords

Acyclovir; Tb- Acyclovir complex; Luminescence intensity; Enhancement

Main Subjects

Analytical chemistry

pH Assists for Sele ctive Determination of Acyclovir by the Emission Enhancement of Tb^{3+}Chemosensor in Tablet and Serum Samples

1. Introduction

Acyclovir (A.C.V.) 2 - Amino - 1,9 - dihydro - 9-((2-hydroxyethoxy) methyl) -3*H*-purin-6-one ($C_8H_{11}N_5O_3$), Figure (4.1), it is an anti-viral drug, its Action is by converted to Acyclovir monophosphate by virus-specific thymidine kinase then converted to thymidine triphosphate by other cellular enzymes. Dosages: for adults 400 or 200 mg/day 5days [1]. Several assay methods have been reported for the determination of Acyclovir in biological fluids using capillary electrophoresis [2] or liquid chromatographic methods with pulsed amperometric detection [3], tandem mass spectrometry [4], fluorescence detection [5-7] or ultraviolet detection [8- 15]. In the published methods, liquid-liquid extraction with acetonitrile or mixture of isopropyl alcohol and dichloromethane as the solvent has been used for sample preparation [4, 8, 9]. The disadvantage of these methods employing liquid-liquid extraction (with grate chemical consumption) of Acyclovir from biological fluids is that they involve several steps yielding poor separation from the endogenous serum interferences. In the present work, the chemosensor Tb^{3+} ion in DMSO and at pH 10 is used for sensitive determination of Acyclovir in serum and tablet samples. We determined acyclovir concentration in blood serum by luminescence enhancement of this chemosensor. This is a relatively simple and inexpensive technique providing a quick reproducible analysis and is relatively free from interference with coexisting substances.

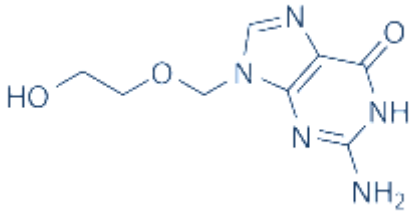

Fig. 1: Structure of Acyclovir

2. Experimental

2.1. Materials

Pure standard Acyclovir supplied by the National Organization for Drug Control and Research (Giza, Egypt). Pharmaceutical preparation (Acyclovir) containing 400 mg/tablets of Acyclovir produced by Misr Company for pharmaceuticals.

4.2.2 Reagents

All solvents were purchased from Sigma–Aldrich. All chemicals used are of analytical grade, and the solvents (Dimethyl sulfoxide, dimethylformamide, acetonitrile, and ethanol) are of HPLC grade. In the present investigation. The materials NH_4OH, H.C.L., and Terbium nitrate were purchased from Sigma–Aldrich. A stock solution ($1x10^{-2}$ mol L^{-1}) of Acyclovir was prepared by exact weighing and dissolution in absolute acetonitrile. A stock solution (1.0×10^{-2} mol L^{-1}) of $Tb^{3+}$was freshly prepared by dissolving 0.0109g $Tb(NO_3)_3.5H_2O$ (delivered from Aldrich-99.99%) in a small amount of Ethanol in 25 mL measuring flask, then dilute to the mark with the same solvent. The working solution of Tb^{3+} ion is of 1.0×10^{-4} mol L^{-1} was obtained by appropriate dilution of appropriated solvent. The pH of the working solution was adjusted to 4 and 10.7 for Acyclovir, by using 0.1 mol L^{-1} of NaOH and/or 0.1 mol L^{-1} of HCl solutions.

The Tb^{3+} complex was prepared by transferring 0.1 ml aliquots of the drug working standard solution into a 5 ml volumetric followed by adding the required volume of Tb^{3+} solution. The solutions were then shaken vigorously before measuring their absorptions and luminescence spectra. Stock and working solutions are stored at 20^oC when they are not in use.

2.3 Apparatus

All Luminescence measurements were carried out on a Meslo-PN (222-263000) z Thermo Scientific Lumina fluorescence spectrometer equipped with a 150 W Xenon lamp source quartz cells of 1 cm path length. The slit widths of excitation and emission wavelength were 10nm/10nm, and the range of wavelength was (400 – 720 nm). All absorption spectra were performed on a Thermo UV-visible double beam spectrophotometer equipped with quartz cells (200-800nm). The separation of serum in samples was carried out by centrifuging of sample for 15 min at 4000 rpm on thermo scientific 300 centrifuges.

2.4 General Procedure

Preparation of lanthanide complex Tb^{3+}- Acyclovir solution: To 10 mL measuring flasks, solutions were added in the following order: 0.1 mL of 1.0×10^{-2} mol L^{-1} $Tb(NO_3)_3$ solution and 0.3 mL of 1.0×10^{-2} mol L^{-1} acyclovir solution to give 1.0×10^{-4} mol L^{-1} of $Tb(NO_3)_3$ and 0.3×10^{-4} mol L^{-1} of Acyclovir. The mixture was diluted to the mark with DMSO. 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 $\lambda_{ex}/\lambda_{em}$ =320/545 nm. The U.V. absorption spectra were measured in the range of (200-800nm).

2. 5. Calibration curve:

After preparing the different standard solutions of Acyclovir in DMSO as described above, the chemosensor Tb^{3+} was mixed with the standard solution of Acyclovir in the cell of the spectrofluorimetric device. Then the luminescence spectrum was measured at the selected excitation wavelength λ_{ex} = 320 nm.

2. 6. Determination of Acyclovir in pharmaceutical preparations

One tablet of pharmaceutical formulation Acyclovir 400 mg was carefully weighed and ground to finely divided powders. Accurate weights equivalent to 3.5 $x10^{-2}$ mol L^{-1} was dissolved in 50 mL DMSO and mixed well and filtered up using 12 mm filter papers. The concentration of the drug was determined by using different concentrations from the corresponding calibration graph.

2.7. Preparation of serum samples

The whole blood samples were collected from patients in the Egyptian police hospital in Serum Separator Tube (S.S.T.) - This tube contains a clot activator and serum gel separator. It has no anticoagulant, centrifuged for 10 min at 4000 rpm to obtain the separated serum available for analysis after decantation, 0.1 ml of serum was added to 1x 10^{-7} mol. L^{-1} of drug and 1.5 ml of 1x 10^{-4} of the Tb(III) sensor in 1.0 cm cell and the luminescence intensity was measured at $\lambda_{ex}/\lambda_{em}$=320/545 nm.

3. Result and discussion

3.1 Absorption and emission spectra

The absorption spectrum of Acyclovir with Tb^{3+} complex is shown in Figure 4.2; comparing its spectrum before and after the addition of Tb(III) ion into its solutions in DMSO, a redshift was observed, which indicates that the Acyclovir can form a complex with Tb(III) ion in the ground state.

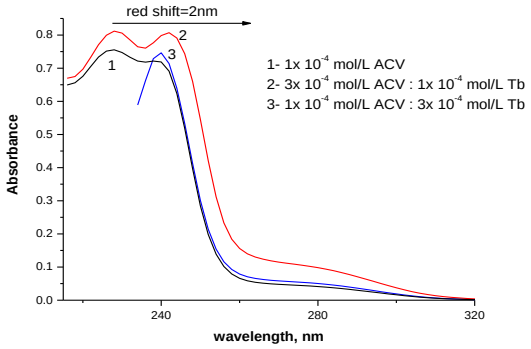

Fig. 4.2: Absorbance spectra of different molar ratios between Tb^{3+} and Acyclovir in DMSO.

3.2. Emission spectra:

The luminescence emission spectra of Tb^{3+} with different concentrations of Acyclovir is shown in Figure (4.3). From curve 1 in Figure 4.3 it can be seen that single Tb^{3+} ion has nearly no peak. After the addition of acyclovir to Tb^{3+} ion, the characteristic peaks of Tb^{3+} ion ($^5D_4 \rightarrow {}^7F_6$=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) were appeared, (see curve 2 in Figure 4.3, which indicates that a good energy transfer from acyclovir to Tb^{+} in its complexes [10-15]. From Figure 4.4 the molar ratio between Tb^{3+} and Acyclovir is 1:3 (metal: ligand), which indicates that the metal may coordinate with the drug from different sites and not only through the oxygen of the ketone ring, but the more preferred coordination sites are the O of the ketone group. Figure 4.5 shows the emission spectra of Tb^{3+} with different concentrations of Acyclovir in DMSO, the intensities of the characteristic peak at 545 nm of Tb^{3+} is enhanced linearly as the concentration of the acyclovir increases indicating that Tb^{3+} ion can be used as a chemosensor for the drug.

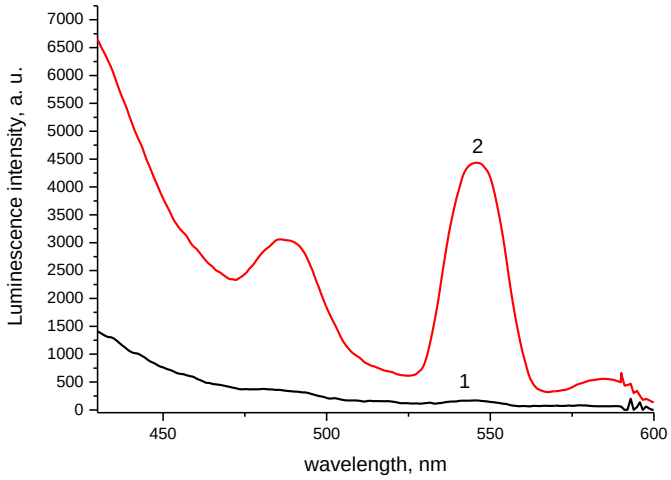

Fig. 4.3: Luminescence spectra of (1): 1 x 10^{-4} mol $L^{-1}Tb^{3+}$ and (2): 1 x 10^{-4} mol L^{-1} Tb^{3+} with 3 x 10^{-4} mol L^{-1} of Acyclovir in DMSO at λ_{ex}=320 nm.

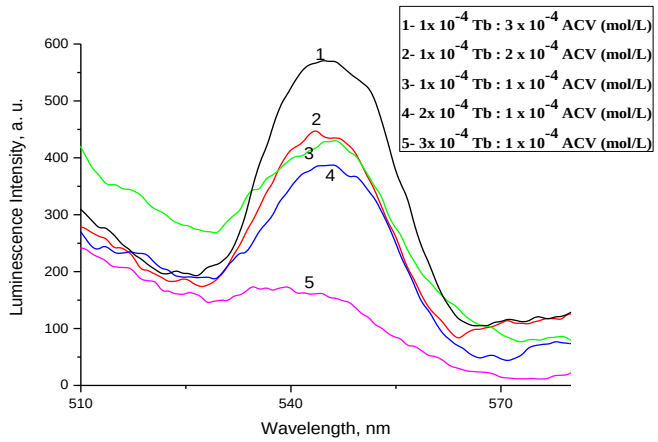

Fig. 4: Luminescence spectra of different Molar ratios between Tb^{3+} and 1 x 10^{-4} mol L^{-1}Acyclovir in DMSO at λ_{ex}=320 nm.

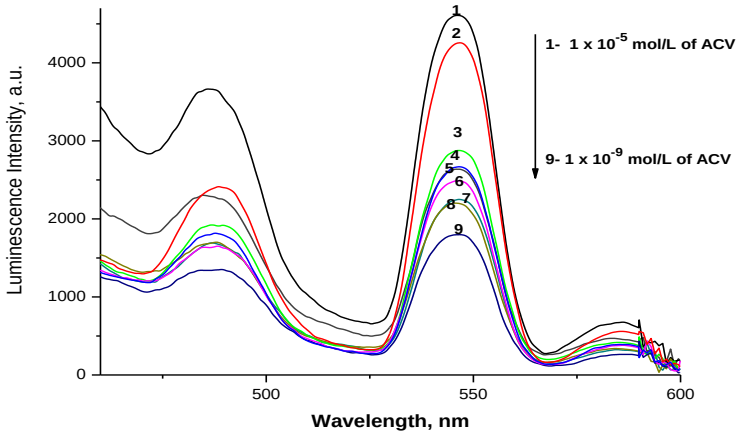

Fig. 5: Luminescence emission spectra of 1 x 10^{-4} mol L^{-1} Tb^{3+} in the presence of different concentrations of ACv in DMSO at pH 10.

3.3. Effect of experimental variables

3.3. 1 Effect of solvent

The influence of the solvent on the luminescence intensities of the solution containing 3.0x10^{-4} mol $L^{-1}$of Acyclovir and 1.0 x10^{-4} mol L^{-1} Tb^{3+} was studied under the conditions studied above .The results show the enhanced emission of Tb^{3+}-Acyclovir in DMSO. This can be attributed to the formation of anhydrous solvates of Tb^{3+}-Acyclovir complex introducing solvent molecules in the first coordination sphere of Tb^{3+}-Acyclovir 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), Figure 4.6.

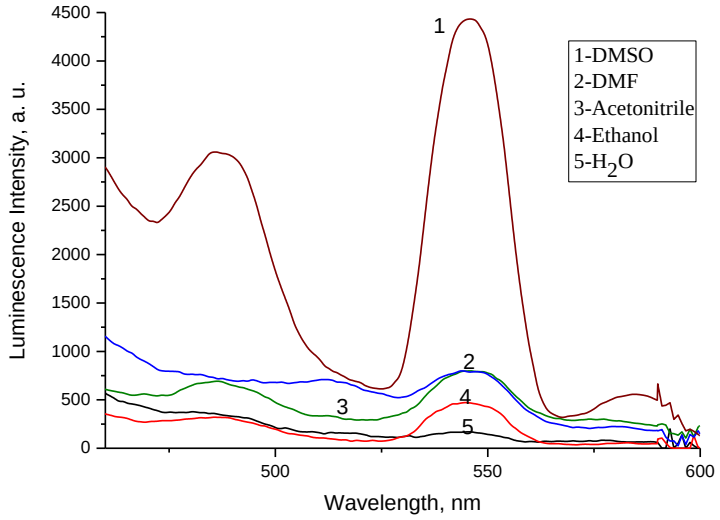

Fig. 6: Luminescence emission spectra of $1x10^{-4}$ mol L^{-1} Tb^{3+} in the presence of $3x10^{-4}$ mol L^{-1} of Acyclovir at pH=10 in different solvents at λ_{ex}=320 nm.

By increasing the radiative rate, Tb^{3+}excited states will become less sensitive to the deactivation process, ultimately resulting in a more efficiently emissive Tb^{3+}complex. Also, the luminescence intensities for the complexes in DMSO solutions are stronger than in ethanol. This may be due to vibrational energy transfer to solvent molecules. It is well known that the excited state of the lanthanide ions is efficiently quenched by interaction with high-energy vibrations like O-H groups. Thereby the luminescence of this complex in –O.H. containing solvents can be quenched easily because of the O-H oscillators. [15-31].

3.3. 2 Effect of pH

The pH of the medium has a significant effect on the luminescence intensity of the Tb^{3+}-ACV complexes. Figure (4.7) show the luminescence intensity of the Tb^{3+}-ACV at different pHs ranged from 3 to 11 using 0.1mol L^{-1} of HCl and /or NaOH. The results obtained show that the maximum luminescence intensity is obtained at pH 10 for (A.C.V.) Therefore, in the subsequent work, the pH of the tested solutions was adjusted by 0.1 mol L^{-1} of HCl and /or NaOH to pH 10 before each measurement.

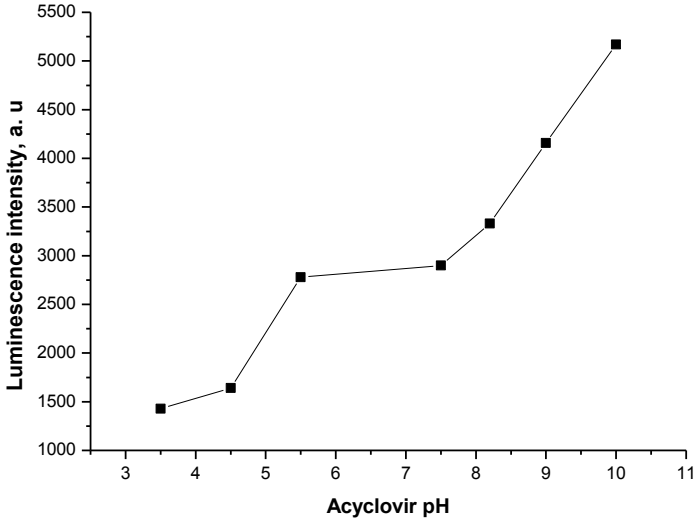

Fig. 4.7: Luminescence emission spectra of $1x10^{-4}$ mol L^{-1} of Tb^{3+} in $3x10^{-4}$ mol L^{-1} Acyclovir in DMSO at different pH at λ_{ex}=320 nm.

3.4. Linearity and validation parameters

3.4. 1 Linearity and range

A linear correlation was found between the luminescence intensity of Acyclovir-Tb^{3+} complex at 545 nm, and the concentration of Acyclovir shown in Figure (4.8). The five points ($1.7x10^{-5}$ to $1.12x10^{-9}$ mol L^{-1}) calibration curve was obtained by plotting the peak intensity of Tb^{3+} at λ_{em}=545 nm versus the concentration of Acyclovir, and the regression equation described the graph Y= a + bX (where Y= luminescence intensity of the optical sensor at λ_{em}=545 nm; a = intercept; b= slope and x = concentration in mol L^{-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 (4.1).