

Chemistry Department Faculty of Science

Modern analytical techniques for early diagnosis of some chronic diseases

Thesis by

Amal Ahmed Mohamed

In Partial Fulfillment of the Requirements for The Degree of Ph.D of Science (Chemistry)

Submited to

Chemistry Department Faculty of Science Ain Shams University **Supervised by**

Prof. Dr. Mohamed Said Attia

Professor of Analytical Chemistry, Faculty of Science, Ain Shams University

Dr. Ahmed Osman Youssef

Associate Professor of Analytical Chemistry, Faculty of Science, Ain Shams University

Prof. Dr. Rasha Hamed El-Sherif

Professor, Faculty of Medicine, Kasr El Ainy Cairo University

Dr. Dinaa Yehia Sabry

Associate Professor of Analytical Chemistry, Faculty of Science, Ain Shams University

(2019)



Chemistry Department Faculty of Science

Approval sheet for submission

Title of Ph.D of Science Thesis

Modern analytical techniques for early d iagnosis of some chronic diseases

By

Amal Ahmed Mohamed

M.Sc. Analytical Chemistry Ain Shams 2015

The thesis has been approved for si	ibmission by the
supervisors:	
Prof. Dr. Mohamed Said Attia	•••••
Professor of Analytical Chemistry,	
Faculty of Science, Ain Shams University	
Dr. Ahmed Osman Youssef	
Associate Professor of Analytical Chemistry,	
Faculty of Science, Ain Shams University	
Prof. Dr. Rasha Hamed El-Sherif	•••••
Professor, Faculty of Medicine, Kasr El Ainy	
Cairo University	
Dr. Dinaa Yehia Sabry	• • • • • • • • • • • • • • • • • • • •
Associate Professor of Analytical Chemistry,	
Faculty of Science, Ain Shams University	
Prof	. Dr. Ayman Ayol
Chairman of C	Chemistry Department

Faculty of Science, Ain Shams University



Chemistry Department Faculty of Science

Modern analytical techniques for early d iagnosis of some chronic diseases

By

Amal Ahmed Mohamed

M.Sc. Analytical Chemistry Ain Shams 2015

The thesis has been approved for susupervisors:	ibmission by the
Prof. Dr.Mahmoud Sabry Mohamed	•••••
Professor of Analytical Chemistry, Faculty of Science, Cairo University	
Dr. Enas Mohamed Ali Abo Taleb	•••••
Professor of Purification of water National R	Research Centre
Prof. Dr. Mohamed Said Attia	•••••
Professor of Analytical Chemistry, Faculty of Science, Ain Shams University	
Dr. Ahmed Osman Youssef	•••••
Associate Professor of Analytical Chemistry, Faculty of Science, Ain Shams University	

Date of examination: / / 2019

CONTENTS

Title		Page
Acknowled Aim of the Abstract Abbreviation List of figuration	work ons ures	i ii iii iv v vi
1.1.	Optical sensors	1
1.2.	Nanoparticles as biochemical sensors	1
1.3.	Fluorescence spectrophotometers	2
1.4.	Lanthanides	2
1.4.1.	Definition of the f elements	2
1.4.2.	Occurrence in nature	3
1.4.3.	Historical perspectives	3
1.4.3.1.	Discovery of lanthanides	3
1.4.4.	Separation of lanthanides	4
1.4.5.	Electron configuration	5
1.4.6.	Physical properties of lanthanides	6
1.4.6.1.	Color and light absorbance	6
1.4.6.2.	Magnetic and spectroscopic properties	7
1.4.7.	Chemical properties of lanthanides	7
1.4.8.	Coordination chemistry of lanthanide ions	8
1.4.9.	Lanthanides chelate	9
1.4.10.	Lanthanides luminescence	9
1.4.11.	Energy transfer	15

1.4.12.	Luminescent lanthanide complexes	17
1.5.	Lanthanides as structural and analytical	18
	luminescent probes	
1.6.	Quenching of luminescence	19
1.6.1.	Types of quenching of luminescence	19
1.6.1.1.	Collisional (dynamic) quenching	19
1.6.1.2.	Static quenching	19
1.6.2.	Theory of collisional quenching	19
1.6.3.	Theory of static quenching	21
1.7.	Solvent effect	22
1.7.1.	Influence of the solvent on the intensity of	23
	absorption spectra	
1.7.2.	Influence of the solvent on the intensity of	24
	luminescence spectra	
1.8.	Applications of lanthanides	25
1.8.1.	Metals and alloys	25
1.8.2.	Non-nuclear	25
1.8.3.	Nuclear	25
1.8.4.	The biological properties of lanthanides	27
1.8.4.1.	Anti cancer agents	28
1.8.4.2.	Osteoporotic treatment	29
1.9.	Chronic disease	29
1.9.1.	A list of chronic diseases	30
1.10.	Literature review	32

Chapter 2

A highly Selective and Sensitive Spectrofluorimetric Method for the Assessment of Folic acid in Pharmaceutical formulation, Serum and Urine by using ${\rm Tb}^{3+}$ - 3 - acetylindole as Optical Sensor

2.1.	Introduction	55
2.2.	Experimental	58
2.2.1.	Materials	58
2.2.2.	Reagents and solutions	58
2.2.3.	Apparatus	59
2.2.4.	General procedure	59
2.2.4.1.	Preparation of lanthanide complex Tb ³⁺ -3-	59
	acetylindole solution	
2.2.4.2.	Calibration curve	60
2.2.5.	Determination of FA in pharmaceutical	60
	preparations	
2.2.6.	Determination of FA in serum samples	60
2.2.7.	Determination of FA in urine samples	61
2.3.	Result and discussion	61
2.3.1.	Absorption and emission spectra	61
2.3.2.	Effect of experimental variables	64
2.3.2.1	Effect of amount of Tb ³ and 3-acetylindole	64
2.3.2.2.	Effect of solvent	64
2.3.2.3.	Effect of pH	65
2.4.	Analytical performance	67
2.4.1.	Analytical parameters of optical sensor method	67

2.4.2.	Selectivity	70
2.4.3.	Application to formulations	72
2.4.4.	Recovery, accuracy and precision study	72
2.5.	Conclusion	76
	Chapter 3	
A new s	ensitive and selective Spectrofluorimetric method fo	r the
Determin	ation of Progesterone, Testosterone and Vitamin D3	using
a High	ly Selective Photo Probe Based on the Quenching of	the
Lumines	cence Intensity of Tb ³⁺ - 3-acetylindole Complex in S	Serum
	Samples	
3.1.	Introduction	77
3.2.	Experimental	81
3.2.1.	Materials	81
3.2.2.	Reagents and solutions	81
3.2.3.	Apparatus	82
3.2.4.	General procedure	82
3.2.4.1.	Preparation of lanthanide complex Tb ³⁺ -3-	82
	acetylindole solution	
3.2.4.2.	Calibration curve	83
3.2.4.3.	Determination of Progesterone, Testosterone and	83
	Vitamin D3 in serum samples	
3.3.	Result and discussion	83
3.3.1.	Absorption and emission spectra	83
3.3.2.	Effect of experimental variables	87
3.3.2.1.	Effect of amount of Tb ³⁺ and 3-acetylindole	87

3.3.2.2.	Effect of solvent	87
3.3.2.3.	Effect of pH	88
3.4.	Analytical performance	89
3.4.1.	Analytical parameters of optical sensor method	89
3.4.2.	Selectivity	94
3.4.3.	Application to formulations	96
3.4.4.	Recovery, accuracy and precision study	96
3.5.	Conclusion	100
	Chapter 4	
Nove	el Spectrofluorimetric Method for the Assessment o	f
Prostate-	Specific Antigen as Tumor Markers for Prostate C	ancer
	by using Eu ³⁺ - Doxycycline as photo probe	
4.1.	Introduction	101
4.2.	Experimental	103
4.2.1.	Materials	103
4.2.2.	Reagents and solutions	103
4.2.3.	Apparatus	104
4.2.4.	General procedure	104
4.2.4.1.	Preparation of lanthanide complex Eu ³⁺ -	104
	Doxycycline solution	
4.2.4.2.	Calibration curve	105
4.2.4.3.	Determination of TPSA & FPSA in serum	105
	samples	
4.3.	Result and discussion	105
4.3.1.	Absorption and emission spectra	105

4.3.2.	Effect of experimental variables	108
4.3.2.1.	Effect of amount of Eu ³⁺ and Doxycycline	108
4.3.2.2.	Effect of solvent	109
4.3.2.3.	Effect of pH	110
4.4.	Analytical performance	111
4.4.1.	Analytical parameters of optical sensor method	111
4.4.2.	Selectivity	115
4.4.3.	Application to formulations	116
4.4.4.	Recovery, accuracy and precision study	116
4.5.	Conclusion	119
	Chapter 5	
Detern	nination of The Carbohydrate Antigen CA 15-3 us	sing a
Highly	y Selective Photo Probe Based on the Quenching o	f the
Lumin	nescence Intensity of Eu ³⁺ - Oxytetracycline Compl	ex in
	Serum Samples	
5.1.	Introduction	120
5.2.	Experimental	122
5.2.1.	Materials	122
5.2.2.	Reagents and solutions	122
5.2.3.	Apparatus	122
5.2.4.	General procedure	123
5.2.4.1.	Preparation of lanthanide complex Eu ³⁺ -	123
	Oxytetracycline solution	
5.2.4.2.	Calibration curve	123
5.2.4.3.	Determination of CA15-3 in serum samples	124

5.3.	Result and discussion	124
5.3.1.	Absorption and emission spectra	124
5.3.2.	Effect of experimental variables	126
5.3.2.1.	Effect of amount of Eu ³⁺ and Oxytetracycline	126
5.3.2.2.	Effect of solvent	127
5.3.2.3.	Effect of pH	129
5.4.	Analytical performance	130
5.4.1.	Analytical parameters of optical sensor method	130
5.4.2.	Selectivity	133
5.4.3.	Application to formulations	133
5.4.4.	Recovery, accuracy and precision study	134
5.5.	Conclusion	136
	Chapter 6	
A highly	selective and sensitive spectrofluorimetric method f	or the
assessmo	ent of warfarin sodium in pharmaceutical formulat	ions,
urine a	nd serum sample by using Eu ³⁺ - ACAC optical Ser	ısor
6.1.	Introduction	137
6.2.	Experimental	139
6.2.1.	Materials	139
6.2.2.	Reagents and solutions	139
6.2.3.	Apparatus	140
6.2.4.	General Procedure	140
6.2.4.1.	Preparation of lanthanide complex Eu ³⁺ -acac	140
	solution	
6.2.4.2.	Calibration curve	141

6.2.5.	Determination of Warfarin in pharmaceutical	142
	preparations	
6.2.6.	Determination of Warfarin in serum solution	142
6.2.7.	Determination of Warfarin in urine solution	142
6.3.	Result and discussion	143
6.3.1.	Absorption and emission spectra	143
6.3.2.	Effect of experimental variables	144
6.3.2.1.	Molar ratio	144
6.3.2.2.	Effect of solvent	145
6.3.2.3.	Effect of pH	146
6.3.2.4.	TEM image	147
6.3.2.5.	X-Ray and IR images	148
6.4.	Analytical performance	149
6.4.1.	Analytical parameters of optical sensor method	149
6.4.2.	Selectivity	151
6.4.3.	Application to formulations	153
6.4.4.	Recovery study	153
6.5.	Conclusion	156
	Conclusion and recommendations	157
	References	158
	English summary	
	Arabic summary	

ACKNOWLEDGMENT

Words are not enough to describe my deep thank to **Prof. Dr. Mohamed Said Attia**, Professor of Analytical chemistry, Faculty of Science, Ain Shams University, for suggesting the point of the research and for managing of this work, his guidance and supervision in the course of the work, and for his stimulating criticisms and help in the preparation of the thesis. Who taught me how I can be a student seeks to research and knowledge, was supportive and did not spare something. I would like to express my deep thanks and gratitude to **Dr. Ahmed Osman Youssef** Associate Professor of Analytical Chemistry, Faculty of Science, Ain Shams University for his valuable help and support throughout the course of this work.

Also, I would like to thanks to **Prof.Dr.Rasha** Hamed El-Sherif and **Dr.Dinaa Yehia Sabry** for their valuable help and support throughout this work.

I offer my thanks and appreciations to all of those who supported me in any respect in the Chemistry Department during the completion of this thesis.

Last but not Least, my thanks are due to my family, especially my mother and my husband, for support and encouragement which gave me the strength to finish this work and a presence next to me in my life.

Amal Ahmed Mohame

AN OF THE WOR