



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس التوثيق الإلكتروني والميكروفيلم

قسم

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



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



MONA MAGHRABY



Ain Shams University

Faculty of Science

Chemistry Department



Synthesis and characterization of novel nanoparticles for medical purposes

A Thesis

Submitted By

Asmaa Mahmoud Youssef Mohamed

(M.Sc. in Applied Chemistry, Helwan University, 2012)

Submitted for the degree of PhD of Science in

Chemistry

Chemistry Department, Faculty of Science, Ain Shams University

Supervisors

Prof. Mohamed Ahmed Mohamed Mekewi

Prof. of Physical Chemistry, Faculty of Science, Ain Shams University

Prof. Mohamed Abd El Hay Ahmed

Prof. of Physical Chemistry, Faculty of Science, Ain Shams University

Assoc. Prof. Michel Fahmy Abd El Messih

Assoc. Prof. of Physical Chemistry, Faculty of Science, Ain Shams University

Assoc. Prof. Howaida Abd Elfatah Elsayed Fadel

Assoc. Prof. of Physiology & Bio-Chemistry, National Institute of Nutrition

2020

Abstract

Nanotechnology has proved its significant effect in drug delivery, recently. In this study, a good use of nanotechnology was made. Five drugs were synthesized in lab in order to remedy diabetes of type 1 and type 2 and to decrease the consequent diabetic inflammation. All of them were of a particle size within the nano-range. The drugs are Zinc oxide nanoparticles (ZnONPs), Zinc Oxide-Insulin nanoparticles (ZnONPs-Insulin) of ratio 1:1, Zinc oxide-Insulin nanoparticles of ratio 1:0.5, Zinc oxide-Insulin nanoparticles of ratio 1:0.25, Zinc oxide-Curcumin nanoparticles (ZnONPS-CurcuminNPs) of ratio 1:10,⁻³ Zinc oxide-Curcumin nanoparticles (ZnONPS-CurcuminNPs) of ratio 1:10⁻⁴ and Zinc oxide-Curcumin nanoparticles of ratio 1:10⁻⁵. The nanomeric drugs were characterized using XRD, HRTEM, FTIR, EDX and surface area to prove a successful adsorption of the reacting particles and identify the shape and size of the reacting particle. A biological experiment was performed using Albino rats to assess the hypoglycemic effect of five prepared drugs plus Curcumin in the nanorange and comparing it with that of Insulin. An oral glucose tolerance test (OGTT) was performed to the experimental rats on the last day of the experiment in order to check the hypoglycemic effect of the prepared drugs with time. Also, blood samples were withdrawn from the experimental rats for performing glycated hemoglobin (HBA1C) analysis. The whole biochemical analysis revealed the effect of the prepared drug samples and the most potent hypoglycemic drug was found to be ZnONPs-Insulin with the ratio 1:1. After sacrificing of experimental animals, their liver and pancreas specimens were taken to be examined for histopathology. It was found that ZnONPs and ZnONPs-CurcuminNPs has the best effect on pancreas and liver specimens.

Key words: Nanotechnology, drug delivery, diabetes, insulin, Zinc oxide (ZnO), Curcumin, hypoglycemic effect, synthesized, nanoparticles.

Aim of Work

Diabetes is a dangerous disorder unless regular medication was adopted as the subsequent inflammation in all body cells does affect the proper function of body organs. So in this study, the desired targets are

1-prevention of insulin comma

The Insulin comma is resulted from not having a sufficient meal before Insulin injection, because of that the idea of using a suitable drug carrier for Insulin was proposed. The Insulin drug carrier extends the period of time in which Insulin is released and therefore avoid comma.

2-Avoiding the painful Insulin injection.

Insulin cannot be orally administered as Insulin will be digested by means of the digestive system. The subcutaneously injection of Insulin allows Insulin to enter blood directly but is painful to some extent. Therefore, the approach of oral Insulin administration is to be considered by finding out an agent that can protect Insulin against digestion or any surrounding affecting factors till passing to blood.

3-Synthesis of new antidiabetic nanomeric compounds which can act as Insulin competitors which can regulate blood glucose and prevent or cure the inflammation.

Acknowledgement

Praise is to **Allah** for helping me overcome all the difficulties I encountered throughout my research journey.

I would like to thank **Prof. Mohamed Ahmed Mekewei** for the fruitful effort in supervising this work, follow-up, guidance and providing me with fruitful advice.

I am much indebted to **Prof. Mohamed Abd El Hay Ahmed** for his invaluable assistance and advice.

My grateful thanks to **Assoc. Prof. Michael Fahmy Abd El Messih** for his help and encouragement.

Great thanks to **Assoc. Prof. Howaida Abd Elfatah Fadel** for her continuous supervision and kind support throughout all steps of this work.

Contents

List of abbreviations	I
List of figures	IV
List of tables	VIII
Chapter 1: Introduction	1
1. Diabetes	1
1.1. Definition of diabetes and classification	1
1.2. Types of diabetes	2
1.3. The signs and symptoms of diabetes	4
2. Insulin	5
2.1. Chemical structure of Insulin	5
2.2. Sugar regulating function of Insulin	6
2.3. Insulin deployment health problems	7
3. Anti-diabetic agents (hypoglycemic agents)	8
3.1. Biguanides	8
3.1.1. Efficacy and Mechanism of action	8
3.1.2. Side effects	9

3.2. Sulphonylureas	9
3.2.1. Efficacy and Mechanism of action	9
3.2.2. Side effects	10
3.3. Glinides	10
3.3.1. Efficacy and Mechanism of action	10
3.3.2. Side effects	11
3.4. Thiazolidinediones	11
3.4.1. Efficacy and Mechanism of action	12
3.4.2. Side effects	12
3.5. Alpha-glucosidase inhibitors	13
3.5.1. Mechanism of action and efficacy	13
3.5.2. Side effects	13
3.6. Dipeptidyl peptidase-4 inhibitors	14
3.6.1. Mechanism of action and efficacy	14
3.6.2. Side effects	14
3.7. Sodium-glucose cotransporter-2 inhibitors	15
3.7.1. Mechanism of action and efficacy	15
3.7.2. Side effects	15

4. Nano medicine	16
4.1. Zinc oxide nano particles	16
4.1.1. ZnO deed as a hypoglycemic agent	18
4.1.2. Toxicity of ZnO in Mammalian Model	20
4.1.3. Literature survey	20
4.2. Curcumin	22
4.2.1. Structure of curcumin	23
4.2.2. How curcumin could function for diabetes	23
4.2.3. Toxicity of curcumin	24
4.2.4. Literature survey	25
4.2.5. Disadvantages of curcumin	27
Chapter 2: Experimental Part	28
1. Materials and Chemicals	28
2.Characterization	29
2.1. Scanning electron microscopy (SEM)	29
2.2. Surface area measurements	29
2.3. Scanning electron microscopy-energy dispersive X-ray analysis (SEM-EDX)	29

2.4. High resolution transmission electron microscopy (HRTEM)	30
2.5. Fourier-transform infrared spectroscopy (FT-IR)	30
2.6. X-ray diffraction (XRD)	30
3. Methodology	31
3.1. preparation of nano-chemical compounds	31
3.1.1. Preparation of zinc oxide nanoparticles particles (ZnONPs)	31
3.1.2. Preparation of ZnO-Curcumin nanoparticles (ZnONPs-curcuminNPs)	31
3.1.3. Preparation of Insulin-ZnONPs compounds	32
3.2. The biological experiment	32
3.2.1. Animals	32
3.2.2. Ethics	32
3.2.3. Experimental part and grouping	33
3.2.4. Biochemical analysis	34
3.2.4.1. Oral glucose tolerance test(OGTT)	34
3.2.4.1.1. Estimating blood glucose level	35
3.2.4.1.1.1. Procedure(Colorimetric enzymatic method)	35
3.2.4.1.1.2. Calculations	36
3.2.4.2. Glycated Hemoglobin (HBA1C) test	36

3.2.4.2.1. Procedure (Ion exchange Resin method)	36
3.2.4.2.2. Calculations	38
3.2.5. Histopathological examinations	38
3.2.6. Statistical analysis	38
Chapter 3: Results and Discussion	39
1. Physicochemical Characterization	39
1.1. Textural properties	39
1.2. EDX and SEM	46
1.2.1. EDX of ZnONPs	46
1.2.2. SEM of ZnONPs	47
1.3. HRTEM	48
1.3.1. ZnONPs-Insulin	48
1.3.2. ZnONPs-CurcuminNPs	49
1.3.3. CurcuminNPs	50
1.4. FT-IR	51
1.4.1. ZnONPs and ZnONPs-Insulin	51
1.4.2. CurcuminNPs and CurcuminNPs- ZnONPs	51
1.5. XRD analysis	61

1.5.1. ZnONPs	61
1.5.2. ZnONPs-Insulin	61
1.5.3. ZnONPs-CurcuminNPs	62
2. Results and discussion of the biological experiment	66
2.1. Biochemical analysis	66
2.1.1. Oral glucose tolerance test (OGTT)	66
2.1.2. Glycosylated hemoglobin (HBA1C) test	67
2.2. Histopathological examination	76
2.2.1. Histopathological examination of liver	76
2.2.2. Histopathological examination of pancreas	90
Summary and conclusion	106
References	109
Arabic summary	

Dedication

To the soul of my respectable father who inspired me with ambition and good morals.....

List of abbreviations

ADI	Acceptable daily intake
BET	Brunauer–Emmett–Teller
BW	Body weight
CTAB	cetyltrimethylammonium bromide
CurcuminNPs	Curcumin nanoparticles
Cys	Cysteine (an amino acid)
DM	Diabetic mellitus
EDX	Energy dispersive X-ray spectroscopy
EFSA	The European Food Safety Authority
FAQ	The food and agriculture organization
FT-IR	Fourier-transform infrared spectroscopy
GHB	Glycosylated hemoglobin
GI	Gastrointestinal
Hb	Hemoglobin
HBA1C	Glycosylated hemoglobin
HFD	High fat diet