

Nanotechnology and Its Applications for Treatment of Retinal Diseases

Essay
Submitted for partial fulfillment of
Master Degree in Ophthalmology

By

Hani Mohamed Gharieb Ibrahim

M.B., B.Ch. Ain Shams University

Supervised by Prof. Dr. Ahmed Abdalla Darwish

Professor of Ophthalmology
Faculty of medicine, Ain Shams University
and

Dr. Mohamed Moghazi Ali Mahgoub

Lecturer of Opthalmology Faculty of medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2008

ACKNOWLEDGEMENT

First and foremost thanks to ALLAH the God of all creatures who allowed and helped me to accomplish this work.

I would like to express my profound gratitude for **Prof. Dr. Ahmed Abdallah Darwish** Prof. of Ophthalmology, Faculty of Medicine, Ain Shams University for his supervision, continuous guidance and encouragement which have been the main factors to complete this work.

I am also deeply grateful to Dr. **Mohamed Moghazi Ali Mahgoub** Lecturer of Ophthalmology, Faculty of Medicine, Ain Shams University for his assistance and encouragement.

I am also delighted to express my deep gratitude and thanks to all my dear professors and colleagues.

Hani Mohamed Gharieb

CONTENTS

CONTENT	Page	
INTRODUCTION	1	
PART I- Nanotechnology		
NANOTECHNOLOGY	5	
What is Nanotechnology?	5	
History of Nanotechnology	6	
Four Generations of nanotechnology	7	
Nanotechnology Segments:	8	
Tools	8	
Materials	8	
Devices	9	
Intelligent Materials and Machines	10	
Nanomaterials	10	
Materials Used in Nanotechnology:	11	
1- Nanoparticles	11	
2- Quantum Dots	12	
3- Dendrimers	13	
4- Fullerenes:	14	
Types of Fullerenes:	15	
a-Buckminsterfullerene	15	
b-Carbon Nanotubes	16	
c-Boron Buckyball	17	
Nanorobots	17	
Nanomedicine	19	
Nanomedicine Taxonomy	22	
PART II- Applications of Nanotechnology		
for Treatment of Retinal Diseases		

APPLICATIONS OF NANOTECHNOLOGY FOR	24
TREATMENT OF RETINAL DISEASES	
Histology of the retina	24
Retinal Degenerative diseases	25
Current Therapies of Retinal Degenerative	29
Diseases	
CHAPTER 1- Targeted Retinal Drug Delivery	
TARGETED RETINAL DRUG DELIVERY	32
(I) Encapsulated Drug Delivery:	33
(A) Liposomes:	34
Thermally Labile Liposomes	36
Phototargeted Angiography (PTA)	39
Phototargeted Occlusion (PTO)	40
Technique of PTO	42
(B) Polymeric nanoparticles:	47
Advantages of NPs	47
Ocular Penetration and Cellular Uptake of	47
NPs	
PLA NPs for Sustained Release of	49
Budesonide	
(C) Nanostructured Silicon:	50
Retisert	52
Medidur	52
(II) Encapsulated Cell Technology (ECT)	53
Advantages of ECT	54
Phase I Trial of CNTF Delivered by ECT	56
Phase II Human Clinical Trials	60
Other applications of ECT	61
(III) Encapsulated DNA delivery	61
Future Drug Delivery Vehicles	64
Pharmacytes	64
Artificial Cells	65
CHAPTER 2- Retinal Tissue Engineering	

RETINAL TISSUE ENGINEERING	66
Cell-Based Therapy	66
Tissue Engineering	69
Biological Scaffolds	70
Three-Dimensional Cell Cultures	72
Retinal Tissue Engineering	75
Stem Cells and Scaffolds	77
From Microtechnology to Nanotechnology	78
CHAPTER 3- Artificial Vision	
ARTIFICIAL VISION	80
The Retinal Implants	80
How the Artificial Retina Works?	81
(I)DOE'S Artificial Retina Project	82
(II) Artificial Silicon Retina (ASR) Microchip	85
The vOICe Vision Technology	87
What does it work?	87
The vOICe and Nanotechnology	91
Comparison against retinal implant	91
Nanoparticle-Based Artificial Retina	92
Nano-optical Switches to Restore Sight	93
SUMMARY	96
REFERENCES	101
ARABIC SUMMARY	1

LIST OF FIGURES

Fig. No.	Figure Title	Page
1	Nanoparticles (Scanning Electron Microscope Image)	12
2	The 3-D Structure of a Dendrimer	13
3	Buckminsterfullerene C ₆₀	16
4	Carbon Nanotube	16
5	Retinal Histology	25
6	Dry Form of ARMD	27
7	Wet Form of ARMD	27
8	A View of the Retina in a Patient who has Retinitis Pigmentosa	28
9	A View of the Fundus of the Eye and of the Retina in a Patient who has Advanced Diabetic Retinopathy	28
10	Laser treatment of wet ARMD	30
11	Cutaway Drawing Showing the Bilayer Structure of a Phospholipid Liposome	34
12	Drug or Dye Encapsulated in a Thermally Labile Liposome at Normal Body Temperature and Following Brief Laser Warming to 41°C	37
13	Electron Microscopy of a Region Immediately Adjacent to a Treated and Occluded CNV	41
14	A Cross-Section Representation of Choroidal-Neovascularization (CNV) with the Phototarget	43

	Liposomes Entering the	
	Choroidal Artery	
15	Different Steps of PTO	45
16	PTA Before Treatment	46
17	PTA After PTO of the Same	46
	Lesion Shown in Fig. 16	
18	The Relative Sizes of Both	53
	Retisert and Medidur	
19	Encapsulated Cell Technology	55
20	The NT-501 Implant	57
21	Intraocular Placement of an NT-	58
	501 Implant	
22	Electron Micrograph Shows the	63
	Minute Scale of DNA	
	Compacted into NPs	
23	Rotating Wall Vessel from	74
0.4	Synthecon.	
24	Micropillars Provide Scaffolding for 3-D Cell Structures	74
25	RPCs Proliferating on a Polymer	76
	Scaffold	, ,
26	How the Artificial Retina Works?	82
27	ASR Implanted in the Sub-retinal	86
	Space	
28	Video Sunglasses, with Convert	88
	Camera above nose	
29	Mechanism of the vOICe Vision	88
	Technology	
30	A molecule that Changes Shape	94
	When Zapped by Light	
	(nanotweezer)	

LIST OF ABBREVIATIONS

AlPcS4 = Aluminium Phthalocyanine Tetrasulfonate

ARMD = Age-Related Macular Degeneration

ASR = Artificial Silicon Retina

BBB = Blood Brain Barrier

BRB = Blood Retinal Barrier

CDN = Compacted DNA Nanoparticle

CNS = Central Nervous System

CNTF = Ciliary Neurotrophic Factor

CNV = Choroidal Neovascularization

2-D = Two-Dimensional

3-D = Three-Dimensional

DDS = Drug Delivery System

DME = Diabetic Macular Edema

DR = Diabetic Retinopathy

DOE = Department Of Energy (USA)

ECT = Encapsulated Cell Therapy

ESEM = Environmental Scanning Electron Microscopy

FDA = Food and Drug Administration (USA)

hESCs = Human Embryonic Stem Cells

MEMS = Microelectromechanical Systems

nm = Nanometer

NNI = National Nanotechnology Initiative

NP = Nanoparticle

PGA = Polyglycolide

PEG = Polyethylene Glycol

PLA = Polylactide

PLGA = Poly(lactide-co-glycolide)

PMMA = Poly(methyl methacrylate)

PTA = Phototargeted Angiography

PTO = Phototargeted Occlusion

QDs = Quantum Dots

RBCs = Red Blood Cells

RP = Retinitis Pigmentosa

RPCS = Retinal Progenitor Cells

RPE = Retinal Pigment Epithelium

UCSF = University of California, San Fransisco

VEGF = Vascular Endothelial Growth Factor