تطبيقات تقنية النانو فى طب العيون

رسالة مقدمة من

الطبيبة / مروة أحمد محمد البغدادي
بكالوريوس الطب و الجراحة
كلية الطب
جامعة عين شمس

توطئة
للحصول على درجة الماجستير في طب و جراحة العيون

تحت اشراف

الأستاذ الدكتور : محمود حمدي ابراهيم
أستاذ طب وجراحة العيون
كلية الطب
جامعة عين شمس

الدكتور: محمد أحمد رشاد
أستاذ مساعد طب وجراحة العيون
كلية الطب
جامعة عين شمس

كلية الطب
جامعة عين شمس
قسم طب و جراحة العيون
القاهرة
مصر
(٢٠١٣)

Ophthalmic Applications of Nanotechnology

Essay
Submitted For Partial Fulfillment of Master Degree in Ophthalmology

By

Marwa Ahmed Alboghdady

M.B., B.Ch.,
Faculty of Medicine-Ain Shams University

Supervised By

Prof.Dr. Mahmoud Hamdi Ibrahim
Professor of Ophthalmology
Faculty of Medicine
Ain shams University

Assistant Prof. Dr. Mohammad Ahmad Rashad
Assistant Prof. of Ophthalmology
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University
Department Of Ophthalmology
Cairo
EGYPT
(2013)

Acknowledgements

It is pleasure to express my deepest gratitude to ***Professor Dr. Mahmoud Hamdi Ibrahim,*** Professor of ophthalmology, Faculty of Medicine, Ain Shams University, for his kind help, kind supervision, endless support, inspiring advices and encouragement throughout this work.

Sincere thanks to ***Assistant Prof. Dr.Mohammad Ahmad Rashad***, Assistant Professor of ophthalmology, Faculty of Medicine, Ain Shams University, for his help and beneficial advices during this work.

List of Contents

List of Figures

List of Figures (Cont.)

List of Figures (Cont.)

List of Tables

Abbreviations

AMD	age related macular degeneration
ARPE-19	human retinal pigment epithelial cells
AS-ODN-s	Antisense-oligonucleotides
AVE	artificial viral envelope
BRB	blood retinal barrier
CBA	chicken-beta actin
CCR3	cell chemokine receptor 3
cDNA	compacted- DNA
CK30-PEG	polyethylene glycol (PEG)-substituted lysine 30-mer
CL	cationic liposomes
CL-OG	cationic liposomes - Oregon green
CL-ICG	cationic liposomes- indocyanine green
CMV	Cytomegalovirus promoter
CNV	choroidal neovascularization
DC-cholesterol	dimethylaminoethane- carbamoylcholesterol)
DOPE	1,2,-dioleoyl-3-phosphatidylethanolamine
DOTAP	1,2-Dioleoyl-3- trimethylammonium propane
FITC	flurescein isothiocyanate
G	generation
GDNF	glial cell line-derived neurotrophic factor

GFAP	glial fibrillary acidic protein
GUVs	Giant unilamellar vesicles
HSA	human serum albumin
HMG1	high mobility group 1 non-histone nuclear protein
HVJ	hemagglutinating virus of Japan
ICG	indocyanine green
IOBA-NHC	normal human conjunctival cells
IRBP	interphotoreceptor retinoid binding protein
kDa	kiloDaliton
LacZ gene	encodes the beta-galactosidase protein
LCA	Leber's congenital amaurosis
MEMS	Microelectromechanical systems
MOP	mouse opsin promoter
NEMS	nanoelectromechanical systems
NMP	normal mouse peripherin /rdsq
OG	Oregon green
P	postnatal day
pDNA	plasmid DNA
PEI2-GNPs	2-kDa polyethylenimine conjugated to gold nanoparticles
PI	post injection day
RDS	retinal degeneration slow protein

RGCs	retinal ganglion cells
Rh	Rhodamine
RPE65	RPE-specific protein 65 KDa
SEAP	secreted alkaline phosphatase
SOD1	Superoxide Dismutase1 enzyme
SV	simian virus
TGF-β2	transforming growth factor–β2
TMAG	N-αtrimethylammonioacetyl- didodecyl-D-glutamate)
VMD2	RPE-specific vitelliform macular dystrophy 2
VEGF	vascular endothelial growth factor

Definition

Nanotechnology (Greek word nano means 'dwarf') is the creation and utilization of materials, devices, and systems through the control of matter on the nanometer lengthscale, i.e., at the level of atoms, molecules, and supramolecular structures. It is the popular term for the construction and utilization of functional structures with at least one characteristic dimension measured in nanometer scale. A nanometer (nm) is one billionth of a meter (10^{-9}m).This is roughly four times the diameter of an individual atom and the bond between two individual atoms is 0.15nm long. (Table 1) ***(Jain, 2008) and (Zarbin et al., 2012)*.**

Object	Dimension (nm)
Width of a hair	50,000
Vesicle in a cell	200
Bacterium	1,000
Virus	100
Exosomes (nanovesicles shed by dendritic cells)	65–100
Width of DNA	2.5
Ribosome	2–4
A base pair in human genome	0.4
Amino acid (e.g., tryptophan, the largest)	1.2 (longest measurement)
Aspirin molecule	1
An individual atom	0.25

Table (1): Dimensions of various objects in nanoscale ***(Jain, 2008).***

Nanotechnology is not in itself a single emerging scientific discipline. It is a meeting of traditional sciences such as chemistry, physics, materials science, and biology to bring together the required collective expertise needed to develop these novel technologies ***(Shrivastava and Dash, 2009).***

Nanomedicine is a subfield of nanotechnology. It has been defined as ‘‘the monitoring, repair, construction, and control of human biological systems at the molecular level, using engineered nanodevices and nanostructures *(**Morrow and Bawa, 2007**).*

This term was used in publications in1998 ***(Jain, 2008).***

Table 2 lists the historical landmarks in the evolution of nanomedicine.

Year	Landmark
1905	Einstein published a paper that estimated the diameter of a sugar molecule as about 1 nm
1931	Max Knoll and Ernst Ruska discovered the electron microscope—enables subnanomolar imaging
1959	Nobel Laureate Richard Feynman gave a lecture entitled “There’s Plenty of Room at the Bottom,” at the Annual Meeting of the American Physical Society. He outlined the principle of manipulating individual atoms using larger machines to manufacture increasingly smaller machines
1974	Norio Tanaguchi of Japan coined the word “nanotechnology”

1979	Colloidal gold nanoparticles used as electron-dense probes in electron microscopy and immunocytochemistry
1981	Conception of the idea of designing molecular machines analogous to enzymes and ribosomes
1987	Cancer targeting with nanoparticles coated with monoclonal antibodies
1988	Maturation of the field of supramolecular chemistry relevant to nanotechnology:construction of artificial molecules that interact with each other leading to award of the Nobel prize .
1990	Atoms visualized by the scanning tunneling microscope discovered in the 1980s at the international business corporation Zürich Laboratory (Zürich, Switzerland), which led to the award of a Nobel Prize
1991	Discovery of carbon nanotubes
1995	Food and drug assosiation approved Doxil, a liposomal formulation of doxorubicin, as an intravenous chemotherapy agent for Kaposi's sarcoma. Drug carried by nanosize liposomes is less toxic with targeted delivery
1998	First use of nanocrystals as biological labels, which were shown to be superior to existing fluorophores
2000	First food and drug approval of a product incorporating the NanoCrystal R _ technology (Elan, King of Prussia, PA, USA), a solid-dose formulation of the immunosuppressant sirolimus—Rapamune R _ Wyeth)
2003	National Nanotechnology Initiative announced in the United States.
2003	The United States Senate passed the Nanotechnology Research and Development Act,making the National Nanotechnology Initiative a legal entity, and authorized.
2005	Food and drug association approved AbraxaneTM, a taxane based on nanotechnology, for the treatment of breast cancer. The nanoparticle form of the drug overcomes insolubility

Table (2): The historical landmarks in the evolution of nanomedicine ***(Jain, 2008).***