Applications of Nanotechnology in Ophthalmology

Essay
Submitted for partial fulfillment of Master Degree in Ophthalmology

By

ABEER ABD ELWAHAB ABD ELHAKEEM ETMAN
M.B., B.Ch,
Cairo University

Supervised by

Prof. Dr. HAZEM HOSNY NOUH
Professor of Ophthalmology
Faculty of medicine, Ain Shams University

Dr. MOMEN MAHMOUD HAMDY
Lecturer of Ophthalmology
Faculty of medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
Cairo
2012

Acknowledgment

I would like to owe special thanks to ***Prof. Dr.*** **HAZEM HOSNY NOUH,** Professor of Ophthalmology, who initiated and assigned this work and for his generous encouragement through the course of the study.

I wish to express my deepest appreciation and profound gratitude to ***Dr. MOMEN MAHMOUD HAMDY,*** Lecturer of Ophthalmology, for his assistance, kind advice and sincere guidance throughout the course of the study and for his meticulous reviewing and invaluable support.

Abeer Etman

Dedication

I wish to express my deepest appreciation and profound gratitude and to dedicate this work to my **Father and my Mother** for their great support and encouragement all through the way.

List of Contents

List of abbreviations

(3D)	Three-Dimensional
(AFM)	Atomic Force Microscope
(AIDS)	Acquired immune deficiency syndrome
(AMD)	Age-related Macular Degeneration
(AS-ODNs)	Antisense Oligonucleotides
(BRB)	Blood Retinal Barrier
(CDs)	Cyclodextrins
(CdTe)	Cadmium Tellurium
(CMV)	Cytomegalvirus
(CNTs)	Carbon Nanotubes
(CNV)	Choroidal Neovascularization
(CS)	Chitosan
(CsA)	Cyclosporine A
(DDS)	Drug Delivery Systems
(DNA)	DesoxyriboNucleic Acid
(DR)	Diabetic Retinopathy
(ECM)	Extracellular Matrix
(FDA)	Food and Drug Administration
(FLU)	Flurbiprofen
(Fs)	Femtoseconds
(GCV)	Ganciclovir
(Gd)	Gadolinium
(HA)	Hyaluronic Acid
(HCE)	Human Corneal Epithelial cells
(HIV)	Human immunodeficiency virus
(IOL)	IntraOcular lens

(K5)	Plasminogen Kringle 5
(LASIK)	Laser-Assisted In Situ Keratomileusis
(M/NEMS)	Micro- and Nano-ElectroMechanical Systems
(MPS)	Monolayer phagocytic cells
(MRI)	Magnetic Resonance Imaging
(Nd)	Neodymium
(NIR)	Near-infrared
(NPs)	Nanoparticles
(NSAID)	Non-Steroidal Anti-inflammatory Drug
(NV)	NeoVascularization
(OIR)	Oxygen-Induced Retinopathy
(OCT)	Optical Coherence Tomography
(PAMAM)	Polyamidoamine
(PCO)	Posterior Capsular Opacification
(PECL)	Poly-E-CaproLactone
(PEDF)	Pigment Epithelium Derived Factor
(pGFP)	Plasmid Encoding For Green Fluorescent Protein Oligomers
(PIBCA)	Poly Isobutyl-CyanoAcrylate
(PLA)	Poly-D-lactic Acid / polylactide
(PLGA)	Poly(Lactic-Co-Glycolic Acid)
(PMNs)	Polymorpho nuclear leukocytes
(rAAV)	RecombinantAdeno-Associated Virus
(RB)	Retinoblastoma
(RGC)	Retinal Ganglion Cell
(RNAi)	RNA interference
(RNV)	Retinal Neovascularization
(ROS)	Reactive oxygen species

(RP)	Retinitis pigmentosa
(RPE)	Retinal Pigment Epithelium
(siRNA)	Small Interfering RNA
(SLNs)	Solid Lipid Nanoparticles
(SPIO)	Superparamagnetic Iron Oxide
(STM)	Scanning Tunneling Microscope
(TiO_2)	Titanium dioxide
(USPIO)	Ultrasmall Super-Paramagnetic Oxide
(VEGF)	Vascular Endothelial Growth Factor

List of Figures

Introduction

Nanotechnology is the design, characterization, production and application of structures, devices and systems by controlling shape and size at nanometer scale. A nanometer (nm) is one-billionth (10^{-9} m) a meter ***(Zarbin et al., 2010).***

Nanodelivery of drugs is the most obvious application of nanomedicine. Nanoparticles are carrier systems that can be used to deliver genes efficiently to cells. It can also improve the efficacy of drug delivery by overcoming diffusion barriers permitting reduced dosing as well as sustained delivery. These features are attractive for drug treatment of chronic ophthalmic conditions and other conditions associated with cell proliferation, such as ocular neovascularization ***(Zarbin et al., 2010).***

A novel system, based on biosensor DNA tethered to a nanoparticle, was developed for the treatment of retinopathies as Reactive oxygen species (ROS) are thought to contribute to cause many retinal diseases. This approach has the potential to allow the endothelial cells of the retinal vasculature to prevent or treat themselves after hyperoxic insult ***(Prow et al., 2006).***

Tremendous progress in nanotechnology has led to the development of nanometer-sized devices that have recently been tested in many cancer diagnostic and therapeutic applications ***(Nair et al., 2008).***

Retinal degenerative diseases will have promising solutions via nanotechnology through regenerative nanomedicine. Control of features down to the submicron level is achieved readily by biodegradable scaffolds with the proper nano scale features might improve cell survival and differentiation. The nanosurgical ophthalmic operating theater is in its infancy holding many promises in ophthalmology ***(Zarbin et al., 2010).***

The use of nanomaterials for biomedical imaging has been reviewed thoroughly as targeted diagnostic magnetic resonance imaging contrast agents. Gold nanoparticles have been used to enhance tumor identification with computed tomography. Super paramagnetic iron oxide nanoparticles and Quantum dots are an alternative labeling material ***(Zarbin et al., 2010).***

Other future applications of nanotechnology include Presbyopia reversal, bacterial elimination and corneal wound healing ***(Myers and Gurwood, 2006).***

What is nanotechnology?

The prefix nano is from the Greek word *nanos* which means dwarf. A **nanometer** is a unit of measure just like feet, inches and miles .By definition, a nanometer is one billionth (10^{-9}) of a meter. ***(Karkare, 2008)***. It refers to matter in the size range of 1–100 nm, but it is often extended to include materials below 1 μm in size ***(Appenzeller, 1991)***.

The term ***nanotechnology*** refers to the ability to measure, design and manipulate materials at atomic, molecular and supra-molecular level in order to understand, create and apply structures and systems with specific functions attributable to their size ***(Appenzeller,1991)***.

The genetic material desoxyribonucleic acid (DNA) is an example of the natural version of nanomaterials. It is composed of four nucleotide bases in sizes ranging in the sub-nanometer scale, and the diameter of the double helix structure of DNA is in the nanometer range ***(Karkare, 2008).***The molecular building blocks of life –proteins, lipids and carbohydrates and their non-biological mimics- are examples of materials having unique properties determined by their size, folding and pattern at the nanoscale ***(Roco and Bainbridge, 2001)***.

Nanotechnology is a new discipline of science and engineering that has led to innovative approaches in many areas of medicine. Its applications in the screening, diagnosis, and treatment of disease are collectively referred to as **nanomedicine** an emerging field that has the potential to revolutionize individual and population-based health this century ***(Zhang et al., 2008)***. It is now possible to provide therapy at a molecular level with the help of nanoparticles, treating diseases and adding to our understanding of their pathogenesis ***(Boulaiz et al., 2011)*** .

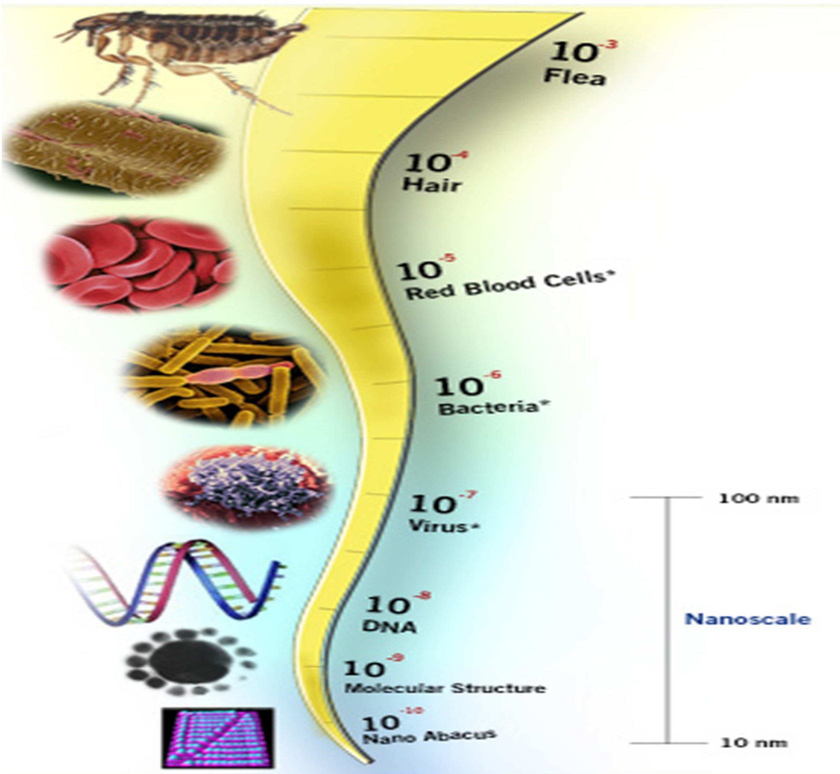

Figure 1: Nanoscale. ***(Cook , 2005).***

Tools used in Nanomaterials visualization

Nanotechnology tools include microscopy techniques and equipment's that permit visualization and manipulation of items at the nanoscale such as cells, bacteria and viruses, and to detect single molecules to better understand the nature of science. The range of tools includes the atomic force microscope (AFM), scanning tunneling microscope (STM), molecular modeling software and various production technologies ***(Gordon and Sagman, 2003).***

These tools use nanoscale probes to image a surface with atomic resolution, and are also capable of picking up, sliding or dragging atoms or molecules around on surfaces to build rudimentary nanostructures. AFM, for example, is routinely used to study biological molecules such as proteins ***(Dowling et al., 2004).***

The fabrication side of nanotechnology has seen the emergence of two paradigms respectively referred as "top down" and "bottom up" ***(Veentra et al.,2004).***

1**-"Top -down"** approach begins with large homogenous objects and removes material as needed to create smaller-scale structures similar to the work of a sculptor in carving a face from a block of marble.

2**-"Bottom-up**" involves putting together smaller components (such as individual atoms and molecules) to form larger and more complex materials.

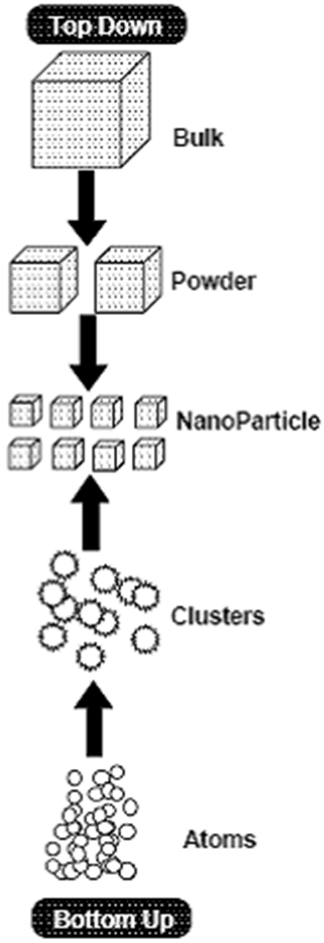

figure2: Top Down and Bottom Up ***(Suneel, 2011).***

Nanomaterials

Nanoscale features

Nanotechnology is not just a simple continuation of miniaturization from micron meter scale to nanometer scale. Materials in the micron meter scale mostly exhibit physical properties the same as the bulk form. However materials in the nanometer scale may exhibit physical properties distinctively different from that of bulk. They exhibit some remarkable specific properties ***(Cao, 2004)***.By creating nanometer scale structures, it is possible to control fundamental properties of materials like their melting temperature, magnetic properties, charge capacity, and even their color ***(Roco et al., 2000)***.

Nanomaterial types

Although a broad definition, some categorize nanomaterials as those which have structured components with at least one dimension less than 100nm. Materials that have one dimension in the nanoscale (and are extended in the other two dimensions) are layers, such as a thin films or surface coatings ***(Dowling et al., 2004).***

Materials that are nanoscale in two dimensions (and extended in one dimension) include nanowires and nanotubes. Carbon nanotubes (CNTs) were first observed by Sumio Iijima in 1991**.** CNTs are extended tubes of rolled graphene sheets (***Dowling et al., 2004).***

Nanowires are ultrafine wires or linear arrays of dots. They can be made from a wide range of materials. They have demonstrated remarkable optical, electronic and magnetic characteristics. The variability and site recognition of biopolymers such as DNA molecules, offer a wide range of opportunities for the self-organization of wire nanostructures into much more complex patterns ***(Roszek et al., 2005).***