THE SCIENCE OF THE MIGHTY 'SMALL': NANOBIO TECHNOLOGY IN HUMAN WELL BEING

KAVITA VASDEV & KRITI TYAGI

Departments of Microbiology, Gargi College, University of Delhi, Siri Fort Road, New Delhi, India

ABSTRACT

Nanotechnology is the design, fabrication and application of structures, devices and systems at the nanoscale dimensions which is about 1 to 100 nanometers. On such an ultra-small scale, these materials demonstrate the unique and interesting properties. Nanotechnology, being inter-disciplinary coalesces various fields of science including quantum physics, biology, chemistry, electrical engineering, computing, materials science, medicine. Nanomaterials including nanoparticles, nanowires, nanofibers and nanotubes have been explored in many biological applications because of the unique properties which differ drastically from their macro scale counterparts. Nanotechnology advancement in biomedical science has proved to be immensely helpful in nanomedicines, targeted drug delivery, diagnostics, therapeutics and tissue engineering. Recently, the development of medical technologies through nano-scale manipulations has seen remarkable growth. In this review, the potential applications of nanotechnology in the field of biology are highlighted.

KEYWORDS: Nanotechnology, Tissue regeneration, Nano particles, Drug Delivery, Quantum Dots & Nanosensors

Received: Nov 24, 2019; **Accepted:** Dec 14, 2019; **Published:** Jan 27, 2020; **Paper Id.:** IJBTRJUN20204

INTRODUCTION

A nanometer is one-billionth of a meter and, the nanoscale comprises of dimensions between 1 and 100 nanometers. Materials reduced to the nanoscale can unexpectedly show very different properties compared to what they display on a macroscale. The “quantum size effect” becomes dominant at this range, which can consequently lead to unusual physical, chemical, and biological properties in materials. For example, copper can turn transparent from opaque; non-reactive material can become a catalyst viz. platinum; solid gold can turn into liquids at room temperature to show size dependent varied colors. Importantly, the smaller a nanoparticle gets, the greater its relative surface area becomes [1]. Together, these effects can greatly affect the catalytic and chemical reactivity of materials. Their size and optical properties can be exploited practically, for instance, nanoscale gold particles [2] accumulate in tumors selectively, where they can enable both detailed imaging as well as targeted laser destruction of the tumor. Nanotechnology, thus, promises to provide the means for designing nanomaterials; materials with customized physical, chemical and biological properties précised by defined molecular structures and dynamics[3]. Nanotechnology encompasses imaging, measuring, creating and manipulating organic and inorganic matter at the nanoscale [4, 5, 6, 7]. Nanotechnology finds huge potential which can provide a platform for much advanced and precise Biological applications [8, 9, 10].

Nanotechnology in Therapeutics Delivery

One of the promising applications of Nano systems is their use as carriers of therapeutics including drug, vaccines, and genes in to the target cell [11, 12, 13, 14, 15]. Nano delivery systems could be multifunctional i.e. they combine targeting, diagnostic, and therapeutic actions at the same time. Release of therapeutics by nano particulate can be

controlled in response to stimuli such as pH, signals such as ultrasound, magnetic fields, near-infrared light, or radiofrequency pulses. Nanoparticles, liposomes, micelles and dendrimers are some of the nano vehicles used as delivery agents that can be prepared to entrap, encapsulate, or bind targeting molecules [16]. These vehicles can improve the solubility, stability, and absorption of several drugs, protecting them from premature inactivation at the same time. Modified C₆₀ fullerenes have shown anti-protease activity against human immune deficiency virus (HIV) and acquired immune deficiency syndrome [17]. It has also been incorporated into drugs designed for the treatment of neurodegenerative disorders because of its powerful antioxidant properties

Nanotechnology could be applied in gene therapy to substitute the currently used viral vectors with potentially less immunogenic nano sized gene carriers [18]. The structure of the nanoparticles protects the nucleic acids from nucleases and the environment; are capable of directing the nucleic acid to the specific location of action; facilitates cell entry and normally sustain gene delivery for longer periods when compared to other vehicles [19]. Many inorganic materials, such as calcium phosphate, gold, carbon materials, silicon oxide, iron oxide, and layered double hydroxide (LDH) have been studied as candidates of gene delivery [20]. Low toxicity and controlled delivery properties of inorganic nanoparticles promises a new alternative to viral and cationic carriers [21, 22]. FUS1 DNA complexed to DOTAP/cholesterol (Chol) nanoliposomes in the mice bearing tumors and metastasis demonstrated the in-vivo antitumor activity. Intravenous and Intratumoral injections of the FUS1 DNA/nanoliposome complex showed significant reduction in the number of metastatic tumor nodules in the mice, by triggering apoptosis consequently leading to cell death [23].

Nanotechnology has opened new vision towards vaccine formulations making them safer, economical, more stable and effective [24]. Adjuvants have been extensively applied to escalate the magnitude of immune responses induced by vaccination. Novel customized nanoparticles as adjuvants with immune modulatory effect can endorse the anticipated types of cellular and humoral immune responses in body. MF59-adjuvanted influenza vaccine is an example of nano-sized vaccine adjuvant, an oil-in-water emulsion composed of about 250-nm droplets has been approved for human use. Immuno stimulating complex (ISCOM) and ISCOM based delivery system with potent adjuvant activity are 40nm cage-like particles produced by combining a protein antigen, cholesterol, phospholipids, and the saponin adjuvant Quil A [25]. ISCOM based vaccines tested with numerous antigens in various experimental models, have shown to be highly immunogenic and capable of eliciting both antibody and cellular immune responses [26].

IMAGING AND DIAGNOSTICS

Nanotechnology has opened up new means in imaging technologies and applications, in medical science. Nanoscience has led to the creation of a new class of visual reporters, known as quantum dots (QDs) that have emerged as a substitute to organic dyes and fluorescent proteins [27]. These colloidal nanoparticles of semiconductors, also known as nanocrystals ranges from of 2–8 nm can withstand iterated cycles of excitation and light emissions. Fluorescence properties of QDs are dependent on their size, shape, composition, and structure. Therefore, QD particles can be made to absorb or emit particular light wavelengths (colors), simply by controlling their size (Figure 1).

Figure 1: The Curves Represent Dependence of Peak Emission Wavelength on QD Diameter, Synthesized from Various Types of Semiconductor Materials [57]. the Range of Emission Wavelength is 400 to 1350 Nm, with Size Varying from 2 To 9.5 Nm. Inset: Shows Emission Spectra for Some of them.

Multi photon microscopy enables high-resolution, efficient multicolor fluorescence imaging of biological samples especially in live tissue as compared to wide-field or confocal microscopy where signals can be imperceptible due to scattering and intrinsic emissions. The QD allow real-time and non-invasive visualization of biological events in vivo as they are easily taken up by cells through endocytosis and can subsequently be used for site-specific intracellular measurements and cellular tracking of biomolecule [28]. QDs can be used as labels for DNA probing of genomic DNA and in fluorescent in situ hybridization assays as well [29]. Semiconductor QDs can allow the detection of hundreds of cancer biomarkers in blood assays, on tissue biopsies, or as contrast agents for imaging [30].

Nanotechnology in Biosensors for Detection and Amplification of Signals

Biological sensors or 'Biosensors' are capable of detecting the concentrations/presence of analyses such water contaminants, pesticides, pathogens. The use of nanomaterials for the construction of biosensors has improved sensitivity and reducing the response-time at the same time. Nanomaterial made tags or labels can be used for pathogen detection in small sample volumes in a highly specific, sensitive, and rapid format at lower costs than conventional diagnostic methods.

Functional electronic, optical, and magnetic nanoparticles bound to bio-molecules like peptides, oligo nucleotides and proteins have been developed for use in biosensors to detect and augment various signals [31]. High number of bio molecules can be immobilized because of the large surface area of nanomaterials, which consequently increases the number of reaction sites obtainable for interaction with a target molecule or species. Detection of very small amounts of a chemical contaminant, virus or bacteria in blood samples or food quality is another potential application of nanotechnology [32, 33].

Thousands of Nanoparticles, either fluorescing different colors or made out of magnetic materials can be placed on a single nanosensor, which can selectively bind to number of food pathogens. This assists in rapid, accurate detection of different bacteria and pathogens even at very low numbers [34]. Also, reducing the pathogen detection time to a few minutes as compared to laborious traditional methods including colony count which ranges from few hours to days [35]. Recently shown Nanosensor can detect the Endocrine disrupting chemicals (EDCs), capable of causing adverse range of

health effects, even at ultra-low levels that too within minutes unlike the previous assays. This sensor system uses non-covalent complexes of gold nanoparticles functionalized with benzyl, as a recognition element and green fluorescence protein (GFP) as a transducer (Figure 2).

Figure 2: Nano Sensor For Endocrine Disrupting Chemicals (EDC) [58]. A) The Sensor Consists of Benzyl Ligand Functionalized Gold (Au) Nanoparticles (Benz NP) and Green Fluorescence Proteins (Gfps). B) When Nanosensor is Added to Cells With and Without EDC Treatment, Benz NP Interacts Differently with the Cell Surface and Releases Different Amount of GFP, Generating Signal Output.

A spectroscopic assay based on Surface Enhanced Raman Spectroscopy (SERS) using silver nanorods, can quickly detect trace levels of viruses with increased sensitivity and specificity. The SERS measures the frequency change of a near-infrared laser as it scatters viral nucleic acids[36]. This frequency change being specifically distinctive enables the spectral difference detection between viruses, their strains, and even viruses with mutations. The method provides a platform for rapid detection and characterization of viruses.

Single-walled carbon nanotube arrays have not only been used for investigating surface-protein and protein-protein binding, but also to develop highly specific electronic biomolecule detectors [37]. Together with the refined nanotube electronic devices, specific electronic sensors for identifying clinically important biomolecules, such as antibodies associated with human autoimmune diseases can be made[38]. Enzyme linked and enzyme free-gold colloids have been used on the surface of electrodes to fabricate biosensors exhibiting high sensitivity, good reproducibility, for the hydrogen peroxide [39,40].

TISSUE ENGINEERING

Tissue engineering (TE) intends to produce biomaterials that matches or mimics the body's own native tissue as much as conceivable. So that, tissues or organs can be produced, restored, and/or replaced using cells, biomaterials, including other biologically active molecules. Most commonly the strategy includes isolation of the specific cells from a patient, growing them on a biomimetic scaffold under carefully measured laboratory culture conditions, implanting the resulting construct in the patient's body at required site, which consequently can direct new tissue development. Organ transplantation in patients

comes with lifelong immune suppressives, increased risk of infections, unwanted side effects and lack of suitable donors. Tissue engineering [41] is a developing field which could help to circumvent these problems. This alternative strategy involves tissues synthesized artificially or naturally, or organ mimics grown on scaffold in the laboratory stimulated by growth factors [42,43] can significantly improve the life expectancy and life quality of thousands of patients around the world. Nanoparticles made from materials such as ceramics, metals like gold and silver, synthetic and natural polymers have made substantial influence on tissue engineering and regenerative medicine [44]. Injectable polymers and nanobiomaterials can serve as good cell support for implant/graft site. Nanotextured materials have shown enhanced cell adhesion properties, stimulating the bone growth very efficiently as compared to previously used traditional materials (Figure 3).

Figure 3: Schematic Representation Displaying the Superiority of Nano Featured Material as Compared to Conventional Materials in Tissue Engineering [59].

The electro spun fibers [45] ranging from 50 to 1000 nm in diameter, show morphologic similarity to the extracellular matrix (ECM) of natural tissue. The pore diameter, porosity, and mechanical properties of such fibers [46] could be customized according to the need. Fabricated scaffolds have shown promising use in bone injuries, and nerve regeneration. Silicone based artificial skin layers, wound dressing made up from new bio-nanomaterials displaying delayed and prolonged release of medicines and nanoparticle (eg silver and gold) dispersions having or loaded with antibacterial properties for direct application, have been explored extensively in skin burn treatments and wound healing [47]. The porcine liver is promising source for liver bioengineering and transplantation is vulnerable to degradation and calcification after harvesting and implantation. Apart from being nontoxic, silver nanoparticles (100 nm) when used as cross-linking of these decellularised liver, have also shown to increase tensile strength, biocompatibility and structural stability as compared to the conventional ones like glutaraldehyde [48]. Studies with Colloidal titania solution for treatment of burn wounds has displayed improved and quicker blood clotting, reduction of wound area much faster with considerable decrease in scar formation and skin color abnormalities [49]. Electric conductivity, chemical stability and sturdiness for employment as scaffolds have made carbon nanotubes a potential material in tissue engineering [50, 51]. Recently, stem cells labeled with multifunctional hybrid mesoporous silica-iron oxide nanoparticles have shown to simultaneously, increase cell viability and retention, guide cell injection in real time, their tracking by magnetic imaging for heart in murine model [52].

CONCLUSIONS

The applications of nanotechnology are far reaching ranging from diagnostics, imaging, and surfactants production, energy production, information technology, telecommunications to tissue engineering [53, 54]. Technology is being rapidly and innovatively explored, it's a result of the quantum effects at nanoscale which allows one to literally fine-tune a material property. Despite the lucrative applications of nanomaterials their impact on environment and living beings has to be critically assessed. Altered properties as compared to their macro particle counterparts and toxicology of many nanomaterials cannot be anticipated. Nanoparticles can enter into human body if inhaled, swallowed, through skin absorption or when intentionally injected during medical procedures [55, 56]. Once inside, they can quickly translocate to vital organs through the bloodstream, can even cross the blood-brain barrier. Carbon black nanoparticles and multi-walled carbon nanotubes toxicities have been implicated in interfering with cell signaling and DNA damages, respectively. Cell damage caused by the Cd-Se quantum dots has also been reported. This necessitates the proper and comprehensive evaluation of the health hazards of engineered nanoparticles, the whole life cycle of these particles needs to be analyzed, including their fabrication, physiological responses, storage, distribution, potential abuse and disposal. Thus, Nanotechnology is a double edged sword which has undoubtedly empowered us but at the same time it raises the concern regarding toxicity and safe disposal which must be and is required to be addressed.

REFERENCES

1. Guo D, Xie G, Luo J. *Applied Physics*. 2013, 47(1):013001.
2. Dreaden E, Alkilany A, Huang X, Murphy C, El-Sayed M. *ChemSoc Rev*. 2012, 41(7):2740-2779.
3. Khan, I.; Saeed, K.; Khan, I. *Arabian Journal of Chemistry*. 2017.
4. Bresme F, Oettel M. *Journal of Physics: Condensed Matter*. 2007, 19(41):413101.
5. Meng X, Seton H, Lu L, Prior I, Thanh N, Song B. *Nanoscale*. 2011, 3(3):977.
6. Chen Y, Cui D. *Nano Biomedicine and Engineering*. 2013, 5(4).
7. Audette, G.; Yaseen, A.; Bragagnolo, N.; Bawa, R. *Biomedicines*. 2019, 7, 46.
8. Bhuyan, D.; Greene, G.; Das, R. *Critical Reviews in Biotechnology* 2019, 39 (6), 759-778.
9. Bamburowicz-Klimkowska M, Poplawska M, Grudzinski I.J *Nanobiotechnol.* 2019, 17:48.
10. Deepak, S, & Kumar, R. *the Role of Nanotechnology to Minimize the Use of Plastic Water Bottles & its Impact on Global Sustainable Environment*.
11. Liu, Y., Lou, C., Yang, H., Shi, M. and Miyoshi, H. *Current Cancer Drug Targets*, 2011,11(2), pp.156-163.
12. Wilczewska, A.; Niemirowicz, K.; Markiewicz, K.; Car, H. *Pharmacological Reports*. 2012, 64 (5), 1020-1037.
13. Dizaj, S., Jafari, S. and Khosroushahi, A. *Nanoscale Research Letters*. 2014. 9(1), p.252.
14. Cho E., Ryu J, Lee H, Hong S, Park H, Hong K, Park S, Kim H, Yoon T. *Journal of Nanobiotechnology*. 2019, 17:19.
15. Le, Q.; Suh, J.; Choi, J.; Park, G.; Lee, J.; Shim, G.; Oh, Y. *ACS Nano*. 2019.
16. Vaughan H, Green J, Tzeng S. *Adv. Mater.* 2019, 1901081
17. Zhu Z, Schuster D, Tuckerman M. *Biochemistry*. 2003, 42(5):1326-1333.

18. Wang J, Hu Z, Xu J, Zhao Y. *NPG Asia Materials*. 2014, 6(2):e84-e84.
19. Yokoyama, M. *Drug Delivery System*. 2006,21(6), pp.615-622.
20. Shabeeb, D. A., Haider, A. J., & Mohammed, A. T. *Synthesis of Gold Nano Particles Using Poly Acrylic Acid as Reducing Agent-Characterization and in Vitro Study of Anticancer Cervix (Hela) Activity*.
21. Kwak, S. *Solid State Ionics*, 2002. 151(1-4), pp.229-234.
22. Jun Loh, X. and Lee, T. *Recent Patents on DNA & Gene Sequences*.2012. 6(2), pp.108-114.
23. Loh, X., Lee, T., Dou, Q. and Deen, G.*Biomaterials Science*. 2016, 4(1), pp.70-86.
24. Ito, I., Ji, L., Tanaka, F., Saito, Y., Gopalan, B., Branch, C., Xu, K., Atkinson, E., Bekele, B., Stephens, L., Minna, J., Roth, J. and Ramesh, R. *Cancer Gene Therapy*.2004, 11(11), pp.733-739.
25. Zhao, L.; Seth, A.; Wibowo, N.; Zhao, C.; Mitter, N.; Yu, C.; Middelberg, A. *Vaccine* 2014, 32 (3), 327-337.
26. Barr I. *Advanced Drug Delivery Reviews*. 1998, 32(3):247-271.
27. Sanders M, Brown L, Deliyannis G, Pearse M. *Immunology and Cell Biology*. 2005, 83(2):119-128.
28. Pisanic II T, Zhang Y, Wang T. *The Analyst*. 2014, 139(12):2968-2981.
29. Joo, K.; Lei, Y.; Lee, C.; Lo, J.; Xie, J.; Hamm-Alvarez, S.; Wang, P. *ACS Nano*. 2008, 2 (8), 1553-1562.
30. Wu, S.; Zhao, X.; Zhang, Z.; Xie, H.; Tian, Z.; Peng, J.; Lu, Z.; Pang, D.; Xie, Z. *ChemPhysChem*. 2006, 7 (5), 1062-1067.
31. Feng Q, Yu M, Kiviat N. *Critical Reviews in Clinical Laboratory Sciences*. 2006, 43(5-6):497-560.
32. Sirisha, V. L., & Campus, K. (2015). *Polysaccharide nanoparticles: preparation and their potential application as drug delivery systems*. *Int J Res Appl Nat Soc Sci (IMPACT IJIRANSS)*, 3, 69-94.
33. Sapsford K, Pons T, Medintz I, Mattoussi H. *Sensors*. 2006, 6(8):925-953.
34. Hahn M, Tabb J, Krauss T. *Analytical Chemistry*. 2005, 77(15):4861-4869.
35. Zou L, Gu Z, Sun M. *Toxicological & Environmental Chemistry*. 2015, 97(3-4):477-490.
36. Ho P. *Pathology*. 2014, 46:S45.
37. Li X, Rotello V. *Nanomedicine*. 2011, 6(8):1295-1296.
38. Shanmukh, S.; Jones, L.; Driskell, J.; Zhao, Y.; Dluhy, R.; Tripp, R. *Nano Letters*. 2006, 6 (11), 2630-2636.
39. Zhong, J.; Song, L.; Meng, J.; Gao, B.; Chu, W.; Xu, H.; Luo, Y.; Guo, J.; Marcelli, A.; Xie, S.; Wu, Z. *Carbon*. 2009, 47 (4), 967-973.
40. Tilmaciu C, Morris M. *Frontiers in Chemistry*. 2015, 3.
41. Ahirwal G, Mitra C. *Sensors*. 2009, 9(2):881-894.
42. Jayaraman, K. *Nanomedicine: Fate and Fortune in Future to Tailor a Device at a Billionth of a Meter, About Half the Width of a DNA*.
43. Sophia J, Muralidharan G. *Journal of Applied Electrochemistry*. 2015, 45(9):963-971.
44. Jakab K, Marga F, Norotte C, Forgacs G. 2015, 71(1):165-166.
45. Vanleene M. *Journal of Nanomedicine & Nanotechnology*. 2015, 06(01).

46. Mandrycky C, Phong K, Zheng Y. *MRS Communications*. 2017, 7(03):332-347.
47. Fathi-Achachelouei, M.; Knopf-Marques, H.; Ribeiro da Silva, C.; Barthès, J.; Bat, E.; Tezcaner, A.; Vrana, N. *Frontiers in Bioengineering and Biotechnology*. 2019, 7.
48. Greiner, A.; Wendorff, J. *Angewandte Chemie International Edition*. 2007, 46 (30), 5670-5703.
49. Vasita R, Katti D. *International Journal of Nanomedicine*. 2006, 1(1):15-30.
50. Tocco I, Zavan B, Bassetto F, Vindigni V. *Journal of Nanomaterials*. 2012, 2012:1-11.
51. Saleh, T.; Ahmed, E.; Yu, L.; Hussein, K.; Park, K.; Lee, Y.; Kang, B.; Choi, K.; Choi, S.; Kang, K.; Woo, H. *Artificial Cells, Nanomedicine, and Biotechnology*. 2018, 46, 273-284.
52. Seisenbaeva, G.; Fromell, K.; Vinogradov, V.; Terekhov, A.; Pakhomov, A.; Nilsson, B.; Ekdahl, K.; Vinogradov, V.; Kessler, V. *Scientific Reports*. 2017, 7 (1).
53. O'Brien F. *Materials Today*. 2011, 14(3):88-95.
54. Jun I, Han H, Edwards J, Jeon H. *International Journal of Molecular Sciences*. 2018, 19(3):745.
55. Chen, F.; Zhao, E.; Hableel, G.; Hu, T.; Kim, T.; Li, J.; Gonzalez-Pech, N.; Cheng, D.; Lemaster, J.; Xie, Y.; Grassian, V. H., Sen, G. L.; Jokerst, J. V. *ACS Nano*. 2019,13(6)
56. Mohanty C, Arya G, Verma R, Sahoo S. *International Journal of Nanotechnology: Biomedicine*. 2009, 1(1):24-38.
57. Morais M, Martins V, Steffens D, Pranke P, da Costa J. *Biological Applications of Nanobiotechnology*. 2014, 14(1):1007-1017.
58. Ray P, Yu H, Fu P. *Journal of Environmental Science and Health, Part C*. 2009, 27(1):1-35.
59. O'Shaughnessy P, Adamcakova-Dodd A, Altmaier R, Thorne P. *Nanomaterials*. 2014, 4(2):439-453.
60. Michalet X. *Science*. 2005, 307(5709):538-544.
61. Le, N.; Wang, X.; Geng, Y.; Tang, R.; Tonga, G.; Jiang, Z.; Rotello, V. *Chemical Communications*. 2017, 53 (62), 8794-8797.
62. Zhang L, Webster T. *Nano Today*. 2009, 4(1):66-80.

AUTHOR'S PROFILE

Dr. Kriti Tyagi

Assistant Professor, Department of Microbiology, Gargi College, University of Delhi.

Ph.D Biotechnology, AIIMS New Delhi. India

Interest Areas: Infection and immunity, Parasitology.

Dr. Kavita Vasdeva

Associate Professor, Department of Microbiology, Gargi College, University of Delhi

Ph.D Microbiology, University of Delhi, South campus

Interest Areas: Molecular biology, Nanomaterials, Bioremediation, Enzymes