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APPLICATION OF NANOTECHNOLOGY IN BIOMEDICAL ENGINEERING AND MEDICINE: A REVIEW

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Abstract

Nanotechnology (NT) is a convergent field that brings together the fields of physics, chemistry, material science and engineering by working on a scale ranging from 1 to 100 nanometres usually known as nanoscale. Nanotechnology has been employed to the design, fabrication, production, characterization and utilization of many materials including biomaterials and devices whereby at least one dimension that affects the functional behaviour of the products is on the nanometre scale and eventually interacts with the human body at sub-cellular level. In this work, synthesis, and applications of nanotechnology and nanomaterials in Biomedical Engineering (BME) and Medicine were studied. Nanotechnology is highly effective and efficient in vast areas of BME, particularly in drug and gene delivery, biosensors, imaging, artificial implants and tissue engineering, nanorobots for surgery, cancer therapy, diagnostic tools and many more for drastic improvement. The synthesized nanomaterials are categorized into zero, one, two and three dimensional nanostructure nanomaterials and are used for different healthcare delivery. Nanomaterials such quantum dots, nanorods, dendrimers and nanotubes overcome challenges faced by the traditional healthcare delivery with its quite slow rate of performance. The advance potentials of normal drug reduce through the use of nanotechnology. Thus, nanotechnology application will improve techniques for tissue regeneration, gene replacement, nanosurgeries, and drug delivery in developing Medicine and BME fields, and creates tremendous effects in the future through its versatile metabolic means.

Keywords: Nanotechnology, Biomedical Engineering, Medicine, Application, Future

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Introduction

Nanotechnology (NT), a newly promising field in material science, electronics, medical sciences and biomedical engineering (BME) with many applications. It is a convergent discipline that brings dimension, extent of reactivity, mechanism, and metabolic nature in biological system. Nanotechnology exists by operating on a scale ranging from 1 to 100 nanometers usually known as the nanoscale (Kalangutkar, 2015). It can be employed in design and fabrication of devices which can influence the functional behaviour of the

products and interacts with the human body at sub-cellular level for the purpose of effective utilization in healthcare delivery.

In this rapidly growing era, NT is at the cutting edge in characterization of atoms, molecules and macromolecules scale for better enhancement in properties and performance through a technique (Kalangutkar, 2015; Saini, Saini and Sharma, 2010). This nanomanufacturing process introduced a revolution in both fields of BME and

Medicine (Kalangutkar, 2015; Ernest and Shetty, 2005). At nanoscale level, the entirely new physical, chemical, mechanical and structural behaviours exist for nanomaterials because of the small and/or intermediate size to give the desired positive output and apparently overcome any limitation emanating from both traditional diagnostic and therapeutic agents.

Nanotechnology has been reported to be highly effective and efficient in vast applications of both BME and medicine, especially in areas of drug, gene therapy, biosensors, imaging, biomaterial artificial implants and tissue engineering, nanorobots for surgery, cancer therapy, analytical and

diagnostic tools to mention a few, which will drastically increase in efficacy (Saini *et al.*, 2010; Saji *et al.*, 2010; Alagarasi, 2011; Kalangutkar, 2014, 2015; Bhat, *et al.*, 2017). In this study, the synthesis or production of nanomaterial and nanotechnology applications in BME and Medicine with the future trend were examined.

Nanotechnology can be categorized into three (3) groups namely nanomaterials as well as nanodevices (tagged as nanoobjects) and nano manufacturing processes as illustrated in Table 1. This paper focuses on nanoobjects and the various applications in medicine and BME.

Table 1: Three main groups of nanotechnology

S/N	Groups	Examples
1	Nanodevice (ND)	Quantum dot, Photonic crystal and Magnetoresistive Random Access Memory MRAM (Spintronics) etc.
2	Nanomaterial (NM)	Carbon nanotube, Graphene, Fullerene, Nanoparticles, Nanofiber, Nanowire, Nanocomposite and Nanocompound
3	Nano manufacturing processes (NMP)	Nanoimprint, Nanoetching, Fine pitch inkjet and nanocoating

Nanomaterials and its Synthesis

Nanomaterials (NM) are substances that have one or more dimensions between 1 and 100 nm and exhibit novel properties not found in bulk materials of the same composition (Alagarasi, 2011; Malsch, 2002). At this nanoscale level, the chemical, optical, electrical, magnetic and structural properties of materials are unique compared to the micro or macroscale level and possess the potential to create positive impact on different fields of study including electronics and medicine. The small size of the materials apparently leads to a large surface area to volume ratio, thereby increasing the dominance in the surface atoms of the nanoparticles over the interior ones and consequently enhancing greater chemical reactivity and change in the strength of the material (Yamamoto, 2001; Alagarasi, 2011; Ulatowska-jarza *et al.*, 2011).

According to Alagarasi (2011), 'nanomaterials were formed after the creation of the big bang of nanostructures in the meteorites'. Michael Faraday in 1857 produced the colloidal gold particles and then fumed silica nanoparticles were manufactured and sold as substitutes for ultrafine carbon black for reinforcements of rubber in USA and Germany by early 1940s. The synthesized nanomaterials are categorized based on structural patterns into zero, one, two and three dimensions. Nanomaterials are used for different purposes as shown in Figure 1.

Zero dimension (0D) are displayed with length, breadth and heights at a single point; one dimension (1D) having very thin films and surface coatings with the thin films synthesized and applied to biological sensor system, fibre-optic systems, information storage systems and optical devices (Seshan, 2002); two dimension (2D) possess length and

breadth in different directions, while three dimension (3D) have all parameters in 3 directions. Kalangutkar (2015) reported that these materials could be in form of particles, shells, tubes, flakes, wire and films with one or more dimensions as shown on the nanometer scale. Figure 1 and 2 depict some types of nanomaterials including quantum dots, rods, dendrimers and nanotubes that exist in nature. Nanoparticles are synthesized to generate novel medical device, implants and drugs for proper and effective healthcare delivery.

Nanomaterials have been employed in solving many biological challenges such as purification of drinking water, medical diagnostics and treatments, cure for cancer through novel techniques, thus enhanced biomedical approaches in terms of performance and cost effectiveness. The most advanced area of nanotechnology application involves the green synthesis of nanoparticles with unique properties such as phototherapeutics potentials, antimicrobial, regenerative, chemical, magnetic and optical properties (Krolikowska *et al.*, 2003; Bhat *et al.*, 2017; Kalangutkar, 2015).

Figure 1: Categories of nanostructure materials (a) OD spheres and clusters (b) 1D nanofibers, rods and wires (c) 2D films, networks and plates (d) 3D nanomaterials (Kalangutkar, 2015)

Figure 2: Types of nanomaterials (Alagarasi, 2011; Kalangutkar, 2014; Kalangutkar, 2015)

The synthesis of nanomaterials may be achieved by bottom up and/or top down approaches as illustrated in Figure 3. According to Ghosh (2007), 'bottom-up method involves the assemblage or production of nanomaterials from atoms, molecule or

cluster, whereas the top-down approach employs traditional size reduction or microfabrication techniques through cut and mill in order to achieve a desired shape materials into the desired shape and order of a material. Several types of bottom up and top

down techniques have been introduced and explored. They are homogeneous and heterogeneous nucleation processes, aerosol synthesis, spray pyrolysis, template-based synthesis and microemulsion based synthesis for the former approach and thermal cycling as well as attrition are for the latter approach.

Ghosh (2007) reported that, 'attrition generates nanoparticles within the range of 20 nm and several hundred nanometers. Also, both bottom up and top down approaches can be combined during the synthesis process to yield a hybrid product. The desired output (nanoparticles) must possess some unique characteristics in the form of identical shape, size, chemical composition and structure. The qualities of nanomaterials employs in medicine and biomedical engineering depend on non-toxicity, biocompatibility, chemosuppressivity, mechanical properties and ultra high level of purity. These have significantly improved quality, techniques and performance of the biomedical devices, diagnosis, prevention, treatments and safety of

human life (Cao, 2006; Juillerat-Jeannere, 2008).

Surface modifications (physical, chemical and biological techniques) of nanomaterials like silver, titanium, silica, gold and many more improved physical and biochemical properties such as solubility and stability, optical emission, electrical, magnetic and mechanical (bond strength) properties through improvement in surface area to volume without toxic impact (He *et al.*, 2004; Heidenau *et al.*, 2005; Kar *et al.*, 2006; Huang, *et al.*, 2007; Huang *et al.*, 2008; Jones and Grainger, 2009; Karagkiozaki *et al.*, 2009; Saji *et al.*, 2010). Modification of inorganic core nanoparticles with inorganic shells coupled with surface immobilized biomolecules have been reported to improve the optical, magnetic properties and biocompatibility have been reported by Saji *et al.* (2010).

Figure 3: Techniques employed for the synthesis of nanomaterials (Alagarasi, 2011)

Applications of Nanotechnology in Healthcare Delivery

Applications of Nanotechnology in Medicine

Diseases such as multiple sclerosis, diabetes, cardiovascular and inflammatory or infectious diseases (including HIV) constitute a high rate of chronic and complex challenges which apparently call for more medical attention and require several unique approaches. One of the

relevant, efficient as well as effective approach is Nanomedicine (NMe). In medicine, this rapidly-growing field enhances healthcare delivery by introducing and applying more efficient techniques ranging from repairing or replacing worn out cells by drug target and delivery as well as using

nanomaterials or nano electronic biosensors for proper diagnosis, monitoring and treatment of many diseases. This application of nanotechnology in medicine is known as Nanomedicine (Kalangutkar, 2015).

Nanomedicine approach involves building, controlling, monitoring and repairing of human systems with the use of engineered nanostructures and nanoobjects at molecular level (Sahoo, 2005) where the developed nanoobjects interact with body cells or tissues to integrate engineering principles (technology) and biological systems not feasible in the past. Nanomedicine can also be said to be the application of nanotechnology and its functions to health and medicine. Nanomedicine has both potential benefits and risks but the benefits to humankind are more than the risks involved. Nanomedicine offers physicians and patients early detection and prevention of diseases and more so, aids in the reproduction of new tissues or organs to replace damaged or worn out tissues (Nikalje, 2015).

According to Kalangutkar (2014), the research and development in nanomedicine are presented in Table 2 and its application explained in Figure 4. Examples of effective nanomedicine includes the use of nano objects as delivery therapeutic agents' tools to repair genetic and metabolic defects; detection of cancer cells and releasing a drug to kill them, manipulation of drugs by causing change in the chemical, physical, electrical properties and bioactivity of the material as well as making use of magnetic NPs in both fields of biology and medicine (Krishnan, 2010).

Biochemically precipitated magnetite (Fe_3O_4) has been found in the cells of algae, bacteria, birds and mammals for organisms utilization as biogenic magnetite to assess the Earth's magnetic field for orientation and navigation. In stem cell technology, magnetic nanoparticles (MNPs) have been successfully used to isolate and group the stem cells (Wang *et al.*, 2009) and eventually served as a valuable tool in tracking and viewing of stem

cells in order to drive their differentiation into specific cell lineage and ultimately to understand their biology.

Nanomedicine has played a significant role in stem cell research and aims to yield more stem cell-based therapeutics for the prevention, diagnosis and treatment of human diseases in the nearest future (Ricardo and Lino, 2010). More relevant information on the synthesis of nanomaterials in biotechnology and biomedicine have been presented by Blakemore (1975) and Benelmekki (2015).

Nanotechnology and Biomedical Engineering

Nanotechnology is applied in BME with specific purpose of producing engineered nanomaterials for new diagnostic, monitoring and therapeutic modalities (Farokhzad and Langer, 2006; Liu *et al.*, 2007; Peer *et al.*, 2007). It plays an important role in many areas of biomedical engineering such as in tissue engineering (TE), control of drug delivery, advanced medical imaging, gene delivery and therapy, diagnostics, artificial implants and many more specific subfields of BME yet to be introduced, mainly to enhance healthcare delivery in the nearest future (Malsch, 2002; Bhat *et al.*, 2017; Fabrizio, 2017). For instance, the production of nanofilm on the material's surface can improve on the electrical, mechanical, optical and biological (biocompatibility and wettability) properties as well as protection against deterioration (Jaworek *et al.*, 2009).

Three dimension (3D) nanomaterials have been synthesized using methods as described by Fierke *et al.* (2008) and have been used for many purposes. Researchers have also exploited nanofibers and unique polymeric nano-structure to design, as well fabricate devices for drug delivery, scaffolds in TE for repairing or replacing lost or damaged tissues and also microfluidic networks (Saji *et al.*, 2010; Ulatowska-jarza *et al.*, 2011).

Table 2: Three stages of research and development in Nanomedicine (Kalangutkar, 2015)

S/N	Stages	Research and Development Division
1	First	Evolutionary
2	Second	Revolutionary- focusing on radical new nanotechnology techniques
3	Third	Production and application of micro and nano structured objects for research, diagnostics and therapeutics

Figure 4: Nanomedicine applications (Kalangutkar, 2015)

A most recent typical example is the use of TE scaffolds, patches and injectables as potential therapies for Cardiac Myocyte condition (Amezcuca *et al.*, 2016). These newly developed tissue engineered multifunctional and multicomponent nanostructures mimic the natural ones by optimizing biomaterials with much consideration on their geometric structures and allow scientists to gain proper understanding of cell manipulation.

Others such as gold nanoparticle sensor have been synthesized to diagnose lung cancer (Mazzone, 2009). Nanotube-assisted protein deactivation has been introduced and applied for pathogens and cell apoptosis (Joshi *et al.*, 2008). Drug–target interface are mostly designed for implantable devices such as vascular stents, dental implants, orthopaedic implants and musculoskeletal implants for removal of electrodeposition on implant surfaces as well as improve tissue formation.

Mulder *et al.* (2008) has identified targeted nanotherapeutics as an efficient innovation in the treatment of cardiovascular diseases (CVD). Figure 5 displayed NT involved in various interdisciplinary fields of BME.

The NT in BME will eventually bring into existence health, consumer medical goods and electronics in the nearest future whose applications would save so many human lives by effectively and efficiently managing several human diseases. Due to the small size and high surface to volume ratio property of nanoparticles, NT has played some specific roles in oncology such as displaying the affected cells clearly and thus binding to the tumor cells through the help of various functional groups (Nie *et al.*, 2007). In cancer treatment, the early detection of cancer has been reported to provide solutions to patient as reported by NCI Alliance for Nanotechnology.

Traditionally, chemotherapy has been applied to kill cancer cells but most times the drug does not really hit the target and inflicts more harm to the individual. Nanotechnology has recently been introduced as an indispensable method for early detection and treatment of the cancerous cells through passive and active targeting technique which involves intracellular drug concentration of

nanoparticles on cancer cells and normal cells are toxically prevented (Cao, 2006). The NPs have potential for targeted and time-release drugs. In the nearest future, multifunctional nanoparticles would be synthesized for diagnosis, image display and treatment of cancer (Nie *et al.*, 2007). Figure 6 showed the use of nanoparticles called nanoshells for the treatment of cancer.

Figure 5: Biomedical engineering applications using nanotechnology

Figure 6: A type of nanomaterial (nanoshells) used for cancer therapy (Kalangutkar, 2015)

Cardiovascular Diseases (CVD) are heart diseases with high morbidity and mortality in the world. Examples of cardiovascular diseases include arrhythmia and atherosclerosis etc. The CVDs involving the heart and vasculature are one of the major causes of morbidity and mortality in the whole world. Several traditional methods of treating these diseases have been employed in the past

and yet, problems still occur. A novel method employing nanotechnology has been developed for proper detection and treatment of CVDs (McCarthy, 2010). For CVDs, nanotechnology offered positive changes in Tissue Engineering (TE), biosensors and diagnostics, targeted therapeutics and molecular imaging.

In the case of Tissue Engineering (TE), newly designed valves, heart muscle and blood vessel have been used to replace defective ones; for targeted therapeutics, drugs have been delivered where needed; in the area of molecular imaging, smart imaging agents detect diseases and in terms of biosensors and diagnostics, nanodevices as well as implantable sensors have been designed to diagnose healthcare problems inside the body (Arayne *et al.*, 2007). For instance, atherosclerosis is a major concern that usually becomes unnoticed or undetected until the beginning of clinical symptoms. Nanotechnology is applied through the help of nanocarriers drug delivery systems and devices including the mechanical stents bearing the nanomaterials, to treat atherosclerosis. Also, NTs are being applied for *in vivo* and *ex vivo* detection of CVD signals which helps to reduce many problems associated with the diseases (Gundogdu *et al.*, 2014).

Future Perspective

The presence of multifunctional and many properties of nanomaterials, diagnosis, monitoring as well as treatment of human diseases including cancer and CVDs become more possible in Medicine and BME such as the aspect of drug release, ability to determine localization of the agents and efficacy. These approaches in nanomedicine and BME give hope to humans with such diseases and knowing well that the patients will survive after being treated with the nanomaterials. Based on many scientific research reports, some investigations are still on *in vitro* and *in vivo* stages at the moment.

More research from various aspects of health ailments will most definitely help to test such experiments especially on the toxicological risks to its fullness in detecting and treating CVDs and cancer in a better and safer way. The behaviour and impact of nanomaterials on growth of human need are yet to be assessed. Bioencapsulation of sol-gel bio-nanocomposite have been targeted to make unique impact in many biomedical applications such as design of biosensors, biocatalysts like tissue formation and tissue –

regenerative implant. The use of silver and other nanoparticles as bioactive coats of hydroxyapatite can make significant impact on tissue formation and diseases prevention

Conclusion

The advances of NT has made it possible to overcome challenges faced by the traditional methods in quite a slow rate. These potential side effects and many other factors of the normal drug will reduce as better understanding of nanotechnology pops up, thereby, leading to more improved techniques for tissue regeneration, gene replacement, nanosurgeries, and drug delivery as well as scalpel-free surgery techniques in developing both Medicine and BME fields in the future. Hence, improvement in healthcare could be as result of improved diagnostic techniques and devices, targeted drug delivery that avoid of destruction of unwanted side effects, and localized therapy to destroy diseased cells through nanomaterials and nanotechnological advancement. The development of more nanomaterials for active and passive implants in tissue engineering, orthopaedic and dental appliances, biomimetic and biological materials as well as nanosensors and electrodes under skin can impart unique innovation in health care delivery.

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