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Review on Nanoparticles

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Abstract: *Materials having overall dimensions in the Nanoscale, or under 100 nm, are referred to as Nanoparticle. This materials have significant actors in contemporary medicine, with therapeutic uses ragging from contrast agent in imaging to carrier for the transport of drug and gene into malignancies. In fact, there are some situations where using nanoparticles makes it possible to Undertake studies and treatments that would otherwise be however, because of their Nanoparticles pose special environment and socio-economic problem. This study will explore the socioeconomic and environment implications of nanoparticle use as well as significant contributions that nanoparticles have made two model medicine. There are several advantages of nanoparticle for contemporary medicine. In fact, there are some situations where using nanoparticles make it possible to undertake studies and treatments that would otherwise be impossible. however, because of their toxicity in particular, Nanoparticles pose special environment and socio-economic problem, this study will explore the socioeconomic and environmental implications of nanoparticle use as well as the significant contributions that nanoparticles have made two modern medicines.*

Keywords: Nanotoxicology, Nanomaterials, Physiological Properties, Cancer, Nanotechnology, Diagnosis,

I. INTRODUCTION

Since the turn off the century researchers have been studying nanotechnology. Their have been several ground-breaking advancement achieved in the field of nanotechnology since Nobel Laureate Richard P.
Feynman first used the term in this well-known 1956 lecture “There’s Plenty of Room at the bottom” (Feynman, 1960). Materials of all kinds where created at the nanoscale through nanotechnology. Nanoparticles (NPs) are a diverse class of material that comprise compounds that are particulate and Have at least one dimensions 100nm. When scientist discovered that is substance’s size might affect its physiochemical qualities, such as its optical capabilities they understood the significance of this materials. The typical hues of 20-nm gold(Au), platinum (, silver (Ag), and Palladium (Pd) NPs are respectively, wine red, yellowish grey, black, and dark black.
Due to the fact that they are not simple molecules, NPs are made up of the three layers: (a) the surface layer, which maybe functionalized with a wide range of small molecules, icons, surfactants, and polymers. (b) The core, which is basically the centre region of the NP and typical refers to the NP itself (c) The shell layers, which is chemically distinct materials from core in all respects.

1.1 Physicochemical Properties

As a matter of fact, nanomaterial have unique properties to bulk counterpart which impart them beneficial characteristics, ironically, they may also bestow them with unique mechanisms of Toxicity. In general, toxicity has been though to originate from nanomaterial size and surface area, composition Shapes, and so forth as reviewed in the following sections.

1.2 Size and Surface Area of the Particles

Particle size and surface area play a major role in interaction of materials with Biological system. Seemingly, decresing the size of the material leads to an exponential increase in surface area relative to volume, thereby making the nanomaterial surface more reactive on itself and to it’s contious milleu. Of note, particle size and surface area dictate how the system responds to, distributes, and elimination the material [2]. It has been established that various biological mechanism including endocytosis, cellular uptake, and efficiency or particles processing in the endocytic pathway are dependent on size of the material [3,4]. Various researches have evaluated in vitro cytotoxicity of Nps of different size employing various cell type, culture conditions, and exposure time [5,6]. However , their in vivo evaluation is difficult

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owing to their more complex nature in the biological systems and requires more comprehensive understanding of the particles [7] though various author have evaluated their toxicity issue in biological systems employing various in vivo models. In general, the size depends toxicity of Nanoparticles can be attributed to its ability to enter into the biological systems [8] and then modify the structure of various macromolecules [9] thereby interfering with critical biological functions.

1.3 Effect of Particles Shape and Aspect Ratio

There has been theory of major advancement in the understanding of interplay between particle size and shape for development of more efficacious nanomaterial based targeted delivery system nevertheless, this is also reenforce that there untold effects should also be examiner as well depicted in Figure 1, nanomaterials come in varied shapes including fibres, rings spheres, and plans. Shapes dependent toxicity has been reported for myriads of nanoparticles including carbon nanotubes, silica, allotropies, nickel, gold and titanium nanomaterial [10] . Basically, shape depend nanotoxicity influence the membrane wrapping process in vivo during endocytosis or phagocytosis [11]It has been observed that endocytosis of spherical nanoparticles is easier and faster as compared to rod shaped or fibre like Nanoparticles [12] and more importantly shperical nanoparticles are relatively less toxic irrespective of whether they are homogeneous or heterogeneous 13]. Nanospherical nanomaterials are more disposed to flow through capillaries causing other biological consequences. Studies have shown that rod shaped SWCNT can block K+ ion channels two to three more efficiently than spherical carbon fullerenes [14]. Of note the shape depend toxicity of silica allotropies is evident by fact that amorphous silica is used as food additives while as crystalline silica is suspected human carcinogen [15] similarly,it has been shown that uptake of gold nanorods is slower than spherical Nanospheres and uptake of namorods reaches maximum when aspect ratio [16]It has been observed that TiO2 fibers are more cytotoxic than spherical entities.

1.4 Effect of Surface Charge

Surface charge also plays an important role in toxicity of nanoparticles as it largely defines their interactions with the biological systems. Various aspects of nanomaterials such as selective adsorption of nanoparticles [17]. Colloidal behaviour, plasma protein binding, blood-brain barrier integrity, and transmembrane permeability are primarily regulated by surface charge of nanoparticles [18]. Of note, positively charged nanoparticles show significant cellular uptake compared to negatively charged and neutral nanoparticles, owing to their enhanced opsonization by the plasm proteins. Moreover, they have also been shown to induce hemolysis and platelet aggregation [19] owing to which causes severer toxicity to the system. For example the toxicity of dendrimers is influenced by surface charge and it has been observed that positively charged PAMAM dendrimer (G4) exhibit time-dependent toxicity toward zebrafish and mice embryos while anionic PAMAM dendrimer display no toxic manifestations [20]. Similarly positively charged Si nanoparticles (SiNP-NH2) have been shown to be more cytotoxic compared to neutral and negatively charged Si nanoparticles which display minimal to no cytotoxicity issues . Pietroiusti et al. Found that acid functionalized SWCNTs exhibits marked embryo toxic effect compared to pristine SWCNTs in pregnant mice models. It has also been observed that surface charge of nanoparticles alters blood-brain barrier integrity and transmembrane permeability. In this regard, it was found that the negatively charged NPs in the size range of 50 to 500 m permeate skin after dermal administration, whereas no such effects were seen for positively charged and neutral particles irrespective of their sizes. Basically, NPs of 50 nm permeate the skin due to the small size and large specific surface area, whereas 500nm particles permeate the skin because the high number and density of charged groups lead to a high charge concentration that overcomes the skin barrier [21]. As the interactions of NPs with the Biological systems are largely influenced by their surface charge, the research fraternities have employed various amendments to shield or modulate their surface characteristics so as to reduce the their toxic manifestations, a glimpse of which has been provided in the later part of the paper. 4) Effect of Composition and Crystalline Structure

Although it has been emphasized that particle size plays significant role in deciding toxicity of nanoparticles we cannot simply ignore studies exemplifying comparable toxicity for diverse nanoparticles chemistries having the same dimensions. These studies highlights that the composition and crystalline structure of nanoparticles also influence their toxicity issues. In a study by using Griffitt et al[22]. Using zebrafish, daphnids, and algal species as models of various

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level it was observe that Nanosilver and Nanocopper with their soluble Form toxicity in all tested organisms, whereas TiO2 of the same dimensions did not cause any toxicity issues [22], thus emphasizing role of compositions in determining the toxicity of NPs.

1.5 Effect of Aggregations and Concentration

The aggregations states of nanoparticles also influence their toxicities. Basically, the aggregation states of NPs depend on size, surface charge, and composition among others. It has been observe that carbon nanotube are mainly accumulated in liver, spleen, and lungs without manufacturing any acute toxicity but induce cytotoxic effects mostly because of accumulations of aggregates for longer periods[23].

Agglomerated carbon nanotube have more adverse effects then will dispersed carbon nanotube and enhance the pulmonary interstitial fibrosis[24]. Moreover, generally, it has been observer that with increase in the concentrations of nanoparticles, the toxicity decreases at higher concentration.

1.6 Effect OFFICER FACE COATING and Surface Roughness

The surface properties of particles have significant role on toxicity of nanoparticles as they play a critical role in determining the outcome of their interaction with the cells and other biological entities. Surface coating can affect the cytotoxic properties of nanoparticles by changing their physicochemical properties such as magnetic, electric, and optical properties and chemical relativity[25]. And can alter the pharmacokinetics, distribution, accumation, and toxicity of nanoparticles. It has been known that the presence of oxygen, ozone, oxygen radicals and transitions metals on nanoparticle surface leads to the generation of ROS and the induction of inflammation by the system; these certainly influence their associated of toxicities issues. To this end, more specifically, Fubini et al.[26] have shown that the specific cytotoxicity of silica is strongly associated with the occurrence of surface radicals and reactivity oxygen species on their surfaces. However, on the other side coin, surface coating could also be employed to reduce the toxicity issues of the nanoparticles. In general, surface coating can mitigate or eliminate the adverse effects on nanoparticles. In particular, proper surface coating can lead to stabilization of nanoparticle as well as elude release of toxic icons from nanoparticles[27].

1.7 Effect of Solvents/Media

Medium/solvent conditions have been known to affects particle dispersion and agglomerations state of nanoparticles, which in turn have effect on their particular size, thereby influencing the toxicity associated with nanoparticles. It has been observed that particular TiO2, ZnO, or carbon black have significantly greater size in PBS then in water; moreover, it is also in general consensus that NPs display different diameters in biological milieu[28] Accordingly, the toxic effects of nanoparticles show variations depending upon the medium composition in which the nanoparticles are suspended; in another way round, the same nanoparticles exhibit different toxic manifestations when dissolved in different medium[29]. Although, the dispersing agent may improve the physicochemical and solution property of nanomaterials formulations, they may also adversely affects the toxicity of nanomaterials.

II. NANOMEDICINE THERAPEUTICS – NANOMEDICINE IN CANCER THERANOSTICS

Nanotechnology is one of the most rapidly growing field in Biomedical science, which has been smartly used to unravel Various biological challenges recently, nanotechnology has been vastly utilized for diagnosis and treatment of many Diseases including cardiovascular diseases, diabetes, cancer, Bacterial infections neuro -diseases, etc Owing to various above mentioned limitations in the conventional therapeutic strategies, different researche group have focused on developing Nanoscale Agents, including liposomal Nanoparticle, metal nanoparticles, Viral nanoparticles, protein nanoparticles and lipid nanoparticles. It is important to mention that nanoparticles Have considerably improved the diagnostics and therapeutics of various cancer due to small size, ease of fictionization, Enhanced drug loading (due to large surface to volume ratio), Effortless penetration abilities, and improved retention inside Target tissue. Apart from that, excellent biocompatibility, Biodegradability, multifunctional applications including biomaging, bio-sensing, diagnostics and therapeutics, has increased the potential use of these nanomaterials for various biomedical applications. Here we are summarizing several proof-of-concept application of Nanosystems, which are currently FDA approved or

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under clinical trials tabulated in Table1. Although, currently The number of Nanotheranostics agents in clinical trial is less, we Believe that it will expand at a rapid rate very soon after watching their bridge process.

2.1 Nanoparticles in Cancer

Plethora of nanotechnology-based products have widely been used as drug delivery agents in cancer therapy, [30] these products include liposomes, dendrimers, carbon nanotubes, polymeric micelles, magnetic nanoparticles, Solid Lipid Nanoparticles, Quantum dots, etc., fig1. Different nanoparticles possessing peculiar characteristics, different sizes are being used in cancer therapy.

A. Cteristics, Different sizes are being used

Dendrimers having nano-size (<nm diameter) are Spherical polymeric particles. They possess a larger Area for the incorporation of therapeutic ageagent. The conceptualization of dendrimers destroyed the morphology and characteristics of malignant Tumors like;rapid proliferation, specific cell surface Antigen expression, and leaky vasculature. The Synthesis of dendrimers intiates with an ammonia Core which reacts with acrylic acid and fabricates triacid molecules. The newly produced triacid molecule then reacts with Ethylenediamine. To make a tri-anime molecule generally known As (G0) generation 0 product. This generation 0 product then react with acrylic acid to form a Hexa_-acid. This Hexa_acid product further reacts With ethylenediamme to form Hexa-anime (G1) The process goes on changes in reaction with ethylenediamine and acrylic acid continue until the desire result is not achieved. Polyamidoamine shorty known as PAMAM-based dendrimers is the most investigated and widely accepted for therapeutic [31]. The DNA-based Polyamidoamine dendrimers for cancer-cellspecific targeting are well described by Choi et al., Folic acid and Fluorescein coupled dendrimers are Developed by a mechanism named Acetylation to Lessen the drug toxicity [32]

B. Magnetic Nanoparticles

Magnetic nanoparticle transfection method follow A principle developed by a group of scientists named Widder and other in the past 1970s for targeting the drug delivery magnetically. The First therapeutic use of these magnetic nanoparticles for transfection was reported in 12S cells in Mice by Mah and coworkers. Recombinant Single-chain FV antibody fragment-medical Superparanagnetic iron oxide nanopcojugated with Luteinizing hormone are shown hormone are shown to be effective for targeting and imaging breast cancers.

C. Calcium Phosphate Nanoparticles

Calcium phosphate nanoparticles alone or in Conjugation with non-viral vectors Reported tremendous outcomes as drug delivery Agents in cellular gene transfer. Calcium Phosphate nanoparticles are more advantageous Over others because of their low production costs, Biocompatibility, reduced microbial degradation, and storage stability. Moveover, it is biodegradable, Hence it does not cause any serere damage or side Effect at the injection site. It is used as a vehicle To deliver of medication like contacceptive, growth Factor, antibiotics, and improved transfection properties Of cells [34].

D. Gold Nanoparticles

Gold nanoparticles are the intracellular drug Delivery agent and possess unique properties, like; Their size can be controlled very easily, their surface Properties can be modified accordingly, their visible Light extinction behavior makes them feasible to Encounter nanoparticle trajectories in the cells. To target HER2 positive breast carcinoma, antiHER2 functionalized gold-on-silica nano-shells Have been prepared, wipe out the problem of The presence of salt in gold Sodium bromohydride Is used However, sodium bromohydride is Unsuitable for target-specific peptides because It lessens the chemical composition of peptides Hydrazine, dimethyl formamide, sodium Bromhydride are the limitation in the therapeutic Use of gold nanoparticles[35-36].

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E. Silica Nanoparticles

Silica is a prominent component of nature Mterials such as glass, sand, etc . It has been Widely used for thousands of year. Recently, its Biomedicine use has been identified. Silica nanoparticles such as N-(6-aminohexyl) – 3 Aminoproplytrimethoxysilance can effectively Result in the transfection of Cos-1 cells with very Lower toxicity [85]. A group of scientists Gary –Bobo Et al. Reported colorectal cancer cells [37].

F. Fullerenes

They are big carbon-caged molecules typically known as Buckyballs. They are the most promising Anticancer carriers because of their unique physical, Electrical, strucpoperties. Their stability makes them a Very choice candidate for effective and safe drug Delivery to the tumor cells. Similarly, the existence of □ – □□□□□□□□□□□□, they can absorb light, high triplet Yield, and can generate reactive oxygen species Upon illumination. These photo properties make Them suitable for photodynamic therapy of cancer Krishna et al. Reported the photoacoustic and Photothermal properties of polyhydroxy fullerenes For cancer therapy and imaging [38].

G. Nanoparticles in Gene Therapy

The introduction of new genes into cells for the purpose of treating disease by restoring or adding gene expression. Techniques include insertion of retroviral vectors, transfection, homologous recombination, and injection of new genes into the nuclei of single cell embryos. The entire gene therapy process may consist of multiple steps. The new genes may be introduced into proliferating cells vivo (e.g., bone marrow) or in vitro (e.g., filbroblast cultures) and the modified cells transferred to the site where the gene expression is required. Gene therapy may be particularly useful for treating enzyme deficiency diseases, hemoglobinopathies, and leukemias and may also prove useful in restoring drug sensitivity, particulary for leukemia.

Gene therapy refers to a mode of treatment that involves introducing new genes into cells, repairing or replacing existing abnormal genes, or regulating the expression of particular genes (Matar et al., 2015).

There are two types of genes therapy, namely somatic gene therapy and germline gene therapy. In brief, somatic gene therapy involves treating diseases by genetically modifying somatic cells such that the changes made are only limited to the patient (Wang and Gao, 2014). Germline gene therapy, on the other hand, aims to correct genetic disorders in either reproductive cells such asova and sperm or early embryos, and therefore, any genetic alternation introduced via type of gene therapy are inheritable (Nielsen, 1997). Generally, it is possible to accomplish gene therapy by introduced naked DNA into target cells; however, some nucleic acid-based medicines are not able to cross the cellular membrane by simple passive diffusion methods because of the negative charge of large DNA molecules and negative nature of the cellular membrane. Therefore, it is important to use a vector to assist the progress of transferring DNA molecules into the cell. Both somatic gene therapy and germline gene therapy, whether in vitro or vivo, require vectors in order to insert ganes into cell. Vectors are broadly classified as viral vectors (Lundstrom,2003). Due to their nature ability to transduce their own genetic material into host cells, viral vectors have been shown to be a highly efficient delivery system in gene therapy (Bouard et al., 2009). Furthermore, viral vectors possess high packaging capacities of up to 50kb and various types of single –and double-stranded genetic material, which significantly widens their range of therapeutic applications (Mountain , 2000). Cancer (Trepel et al., 2015), neurological disorders (Choong et al.,2015), retinal diseases (Ye et al., 2015), hemophilia (High and Anguela, 2015), and arthritis (Gaoter et al., 2000) are only a small proportion of a vast array of diseases that can be treated using viral vectors. Some of the drawbacks of viral vectors, however, are the difficulty associated with thir scale up and engineering and their tendency to exhibit immunotoxicity (Touchefeu et al., 2010). Nan-viral vectors constitute all form of non-viral delivery systems, ranging from physical methods such electroporation (Dean et al., 2003) ultrasound (Chen and Hwang, 2013) and magnetofection (Plank et al., 2003) to chemically built vehicles such as nanoparticles and polymers. As far as their advantages over viral vectors, not-viral vectors are safer in that they are less likely to cause immune reactions and mutagenesis and are also more cost effective and easier to produce (Rammoorth and Narvekar, 2015). [39]

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III. REVOLUTION IN THERAPY DIAGNOSIS

The unique future of nanoparticles led to their adoptions in a variety of applications. Nanoparticles have a variety of shapes, sizes, and structures. Nanoparticles have Several auspocoous advantages that they are multifunctional, they can deliver hydrophobic compounds, they can target disease cells activity and passively, they have the capacity to prolong The drug's circulation time, they can boost the entrance and accumulations of drug in tumor sites they overcome drug Resistance, the safety and tolerability of drugs, and they assist the improvement of other technologies.[40]

Nanotechnology for Cancer Diagnosis-although nanotechnology has yet to be used in clinical cancer detections, it is already applied in a range of medical tests and screens, such as gold Nanoparticles in home pregnancy test. Nanoparticles are being used to capture cancer biomakers including cancer-associated proteins, circulating tumor DNA (ctDNA), circulating tumor cells (CTC), and Exosomes. [41,42] Antibiotics, small surfaces because of this high surface area-to-volume ratio. Multivalent effects can be obtained by presenting multiple binding ligands to cancer cells, which can improve the specifically and sensitivity of diagnosis. Ligands to cancer cells, which can improve the specificity and sensitivity of diagnosis.43]

Nanotechnology for the Detection of Cancer Biomarkars – A cancer biomarker is a detected biological molecule present in the blood, various tissues, and body fluids including saliva and urine that indicate the presence of Cancer cells in the body. Protein (released a protein or cells surface proteins), carbohydrates,64 or nucleic acid (ct DNA, micro-RNA,etc) are all example of Cancer biomarkers that are secreted by the body of Cancer cell during carcinogensis.66 Measurement of Cancer biomarkar level aids in the early detection of Cancer or tumor or recurrence as well as monitoring of therapeutic efficacy. Nanotechnology provides excellent selectivity and sensitivity as well as capacity to assess numerous target at the same time. Nanoparticles/nanomaterial can be used to improve biosensors and offer more precise targeting. Furthermore, the introduction of nanoparticles increase the surface to volume ratio of biosensors, making them more sensitive to the demand of certain biomolecular diagnostics. The three most frequent nanoparticle probes employed in Cancer diagnosis are Quantum dots (QDs) gold nanoparticles (AuNPs), and polymers (PDs). Different cancer can be used in nanotechnology. The following makers are among the example. [44,45]

3.1 Challenges and Outcomes Challenge

This work identifies the prospects of nanotechnology, whereas the challenges in the application of this technology have been identified to include high toxicity cost of moving from laboratory scale to large scale productions and availability of facilities equipment for routine analysis. Outcomes –

1. Explain the fundamentals principle of nanotechnology and their application to biomedical engineering.
2. Apply engineering and physics concept to the nano scale and Nano continuum domain.
3. Identify and compare state of the arts Nano fabrication method and perform a critical analysis of the research literature.
4. Design processing conditions to engineer function nanomaterials.
5. Evaluate current constratints, such as regulatory, ethical, political, social and economical, encountered when solving problem in living systems.
6. Apply and transfer interdisciplinary system engineering approaches to field of bioand nanotechnology project.
7. Discuss and evaluate State-of-the-art characterzation methods of nanomaterials and determine nanomaterial safety and handling method required during characterization.

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