Ozone and Nanotechnology in Dentistry

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By

Shashikiran N. D., Savita Hadakar, Namrata Gaonkar, Swapnil Taur, Sachin Gugawad, Ankita Maurya and Pradnya Chaudhari

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TABLE OF CONTENTS

LIST OF ILLUSTRATIONS

Part A

Part B

LIST OF TABLES

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PART A

NANOTECHNOLOGY

1

INTRODUCTION

DR. SHASHIKIRAN N. D.

James Clerk Maxwell, early in 1867 proposed an inventive concept of nanotechnology. Nanotechnology is a technology which deals with objects of nanometer size and the particles are referred to as nanoparticles (NPs). While the whole world was looking at making things bigger and bigger, he envisioned sub-microscopic machines with the ability to handle individual atoms and molecules. He called them Maxwell's demons, which are what we call 'Nanorobots' today.

Noble prize-winning physicist Richard Feynman presented a landmark lecture entitled, 'There is plenty of room at the bottom' at the annual meeting of the American Physical Society, in 1959.[1] This lecture would lay the foundations of all the basic concepts of nanotechnology. He talked about all the future possibilities at the atomic or molecular level. He also suggested that nanomachines, nanorobots and nanodevices could be used to produce atomically precise microscopic instrumentation and production tools. In this historic lecture, he concluded by saying 'this is a development which I think cannot be avoided'.[1] Although at that time, all of these were merely ideas, they initiated a new way of thinking. Scientists realised that significant effects could be achieved by manipulating matter at the atomic and molecular levels. Since then, nanotechnology has come a long way in different applications such as supramolecular chemistry, self assembling drug carriers and gene delivery systems, nanoparticles and nanocapsules, antibody technologies, polymer-drug conjugates, materials and therapeutics, polymer-protein and antibody conjugates, dendrimer technologies, emulsification technologies, liposome technology, in situ polymerisation, tissue engineering and repair, molecular imprinting including recent innovations in dental diagnostics, nano-precipitation, nanocrystals, etc.

In the year 2000, RA Freitas Jr., introduced the term ‘nanodentistry’.[2] He developed this new technology in dentistry using nanorobots for orthodontics, dentition regeneration, nanomaterials and robots in dentifrice, also known as dentifrobots. Although most of his ideas remained science fiction at that time, gradually they are being realized into practice. Today many applications of nanoscale technology are known and used in the field of dentistry. ‘Nano’ is derived from the Greek word, which means ‘dwarf’. Nanotechnology can be defined as the science and engineering involved in the design, synthesis, characterisation, and application of materials and devices whose smallest functional organisation in at least one dimension is on the nanometre scale (one-billionth of a metre). Therefore, nanomaterial or a nanodevice can be considered as a particle with a maximum size of 1×10^{-7} m. The term ‘nanotechnology’ was first used in 1974 when Norio Taniguchi, a researcher at the University of Tokyo used it to refer to the ability to engineer materials precisely at the nanometer level.[3] Nanotechnology and the science of nanomaterials have the potential to provide benefits in numerous areas such as the synthesis of new materials with advanced properties, production technology, information technology and electronics, ecology and energy conservation, nano-biosystems, medical appliances, transportation, the economy, etc.

2

REVIEW OF THE LITERATURE

DR. PRADNYA CHAUDHARI

Introduction of the 'nano' world

James Clerk Maxwell (1867) was the first to draw attention towards materials at a molecular level.[4] He suggested manipulation at the atomic level to give characteristic features to the materials which could be helpful in different ways He envisioned sub-microscopic machines with the ability to handle individual atoms and molecules, which he called Maxwell's demons, popularly known as 'Nanorobots' today.

Start of nanodentistry

RA Freitas Jr. (2000) introduced the term 'nanodentistry' in his pioneer articles. In this article he envisioned that Nanodentistry would make possible the maintenance of comprehensive oral health by involving the use of nanomaterials, biotechnology (including tissue engineering) and, ultimately, dental nanorobotics (nanomedicine). He also mentioned that when the first micrometre-sized dental nanorobots could be constructed within 10 to 20 years from that time, these devices would allow precisely controlled oral analgesia, dentition replacement therapy using biologically autologous whole replacement of teeth manufactured during a single office visit, and rapid nanometer scale precision restorative dentistry.[2]

Nanotechnology in the field of diagnosis

Nanotechnology can be used for diagnostic purposes, with higher sensitivity, simplicity and accuracy. In prompt diagnosis of oral cancer and precancerous conditions, this nanotechnology is very helpful.

1. Biosensors

Clark and Lyons (1962) developed the first biosensor, which was an enzyme-based glucose sensor.[5] It uses blood and urine as media for investigations. But limitations with them subsequently led to the use of the alternative media of oral fluid.

Dr. Wong (2011) developed a device to detect oral cancer in saliva at the University of California, Los Angeles (UCLA) Collaborative Oral Fluid Diagnostic Research Laboratory.[6] This is an automated POC device that is designed for the electrochemical detection of multiple salivary proteins and nucleic acids. The product is known as the Oral Fluid Nano Sensor Test (OFNASET).

2. Nanoparticles

Kah et al. (2007) carried out a study which demonstrated the potential of antibody-conjugated gold NPs to target and illuminate cancer cells under a reflectance-based optical imaging system. In particular, they have shown that gold NPs can provide an optical contrast to discriminate between cancerous and normal cells and their conjugation with antibodies also allows them to map the expression of relevant biomarkers for molecular imaging.[7]

3. Biochips

Welgium et al. **(2012)** initiated the work in the field of biochips. It led to the development of a diagnostic cytology-on-a-chip technique that rapidly detects premalignant and malignant cells with high sensitivity and specificity. In their approach, they designed a sensor for the diagnostics of oral squamous cell carcinoma (OSCC), which integrates multiple laboratory processes onto a microfluidic platform in three primary steps. First, an oral-cytology suspension is delivered to the sensor using pressure-driven flow, where any cells larger than the membrane-pore size are retained on the membrane surface. The captured cells are then stained with fluorescent dyes and immunoreagents to distinguish the cytoplasm, nucleus, and cancer biomarkers. In their diagnostic approach, they selected the epidermal growth-factor receptor as the targeted biomarker, since it is overexpressed and well characterised in OSCC and associated with aggressive phenotypes. Finally, the stained cells are subjected to a 3D fluorescence-microscopy scan of the membrane surface. This is followed by automated image analysis using open-source software. The advantage of this approach is the speed at which a diagnosis can be made.[8]

4. Quantum dots (QDs)

Kloepfer et al. (2003) were the first to use QDs for bacterial labelling. Since this pioneering work, the use of QDs has been more widespread and is now used for labelling, detection and quantification of *Mycobacterium bovis, Bacillus Calmette Guérin*, *Escherichia coli* and *Salmonella enterica* and *serovar Typhimurium* as well as for the simultaneous detection of *S. enterica* and *S. typhimurium*.[9]

Chalmers et al. (2007) used QDs as luminescent probes to achieve single-cell resolution of oral bacteria biofilms. Using conjugated polyclonal and monoclonal antibodies bound to the QD surface, they were able to label planktonically grown *Streptococcus gordonii*DL1 cells as well as individual species within mixed-species community biofilms.[10]

Yang et al. (2011) successfully used cell-penetrating peptides to conjugate NIR QDs for cancer diagnostics.[11] In their pioneering approach, they managed to label OSCC with QD conjugates by endocytosis for visual in vivo imaging on a mouse model.

Applications of nanotechnology in the field of preventive dentistry

Enamel is made of hydroxyapatite crystal which has a porous structure. Deposits on tooth surfaces are usually lodged in these porosities and bacterial accumulation and proliferation take place. Nanohydroxyapatite crystals present in toothpaste can penetrate and fill these porosities and thereby reduce the formation of plaque and calculus and also control biofilm formation.

Gatti A. (2004) elaborated on the concept of a nano-toothbrush using colloidal silver or gold in between the toothbrush bristles.[12] It enhances the removal of microbial plaque and calculus and, by doing this, it helps in maintaining good periodontal health.

Jeong et al. (2006) conducted a study named ‘Remineralization potential of new toothpaste containing nano-hydroxyapatite’ and concluded that a toothpaste containing nano-sized hydroxyapatite has the potential to remineralise an incipient caries lesion.[13]

Nanorobotic dentifrice (Dentifrobots)

Jr. Freitas (2000) introduced the concept of nanorobots. Nanorobotic technology is used in toothpaste and mouthwashes in the form of dentifrobots that are useful in monitoring the gingival and tooth surfaces regularly for the removal of harmful materials and calculus.[2]

Tooth repositioning by nanorobots

Nanorobots can be used to manipulate periodontal tissue like gingiva, the alveolar bone and cementum and, thereby, allow the painless corrective movement of misaligned teeth. Evidence suggests that orthodontic tooth movement can be enhanced by supplementing the mechanical forces with electricity.

Davidovitch Z et al (1980) in their animal experiment concluded that when 15-20 micro-amperes of low direct current (dc) was applied to the alveolar bone by modifying the bioelectric potential, osteoblasts and periodontal ligament cells demonstrated increased concentrations of the second messengers cAMP and cGMP.[14] These findings suggest that electric stimulation enhanced cellular enzymatic phosphorylation activities, leading to the synthetic and secretory processes associated with accelerated bone remodelling. However, the intraoral source of the electricity is a major problem that has to be addressed.

Nanotechnology in a hypersensitivity cure

Low (2015) in the study named 'Reduction in Dental Hypersensitivity with Nano-Hydroxyapatite, Potassium Nitrate, Sodium Monoflurophosphate and Antioxidants' showed that a toothpaste containing potassium nitrate, sodium monoflurophosphate, and nano-hydroxyapatite plus antioxidants phloretin, ferulic acid and silymarin, applied daily, significantly decreased the tooth pain of dentin hypersensitivity within a two-day to two-week time period.[15]

Administering local anesthesia with nanorobots

Freitas (2000) elaborated on the concept of nanorobots which are used for local anaesthesia and also where a colloidal suspension with millions of nanorobots is deposited in gingival tissue. These robots reach the pulp via dentinal tubules and their movements are controlled by temperature difference, chemical signalling and by a nanocomputer under the control of the dentist.[2] Once they reach the pulp these nanorobots cease all sensations in that specific tooth and after completion of treatment they can be ordered to rejuvenate the lost sensation. This technology is particularly helpful in anxious and apprehensive patients, as well as in small children, where we can administer local anaesthesia painlessly by using this method.

Applications of nanotechnology in the field of therapeutic dentistry

1. Nanocomposite

The nanofiller particles are incorporated into composite to enhance its restorative properties. Nanocomposites have increased hardness, improved handling properties, better translucency, increased flexural strength and a 50% reduction in polymerisation shrinkage.

Buen et al. (2007) compared the physical properties of nanofilled composite with universal hybrid and microfilled composite and found a higher modulus of elasticity with the nanofilled one with high aesthetic properties.[16]

Niu et al. **(2010)** showed that quaternary ammonium nanoparticles can be added to the composite as an antibacterial agent. The study concluded that the addition of zinc nanoparticles in composite enhances its antibacterial effect and improves the clinical service of the restoration.[17]

Farbod (2010) proved that adhesion of a microorganism and formation of biofilm can be minimised by incorporating titanium dioxide nanoparticles in composite that enhances the hydrophilic activity of the resorption in the study ‘An investigation of super-hydrophilic properties of TiO2/SnO2 Nanocomposite thin films’.[18]

das Neves et al. (2010) studied the physical properties and antibacterial activity of a light-activated composite modified with silver nanoparticles in their study ‘Addition of silver nanoparticles to composite resin: effect on physical and bactericidal properties in vitro’.[19] In this study they concluded that lower concentrations of nanoparticles in modified resin showed comparatively less biofilm growth without compromising the strength in compression and surface roughness.

2. Root canal disinfectants

Several nanoparticles, such as zinc oxide and chitosan, alone or in combination, have been incorporated into root canal sealers in an attempt to disinfect root canals. They had no effect on the flow characteristic of the sealers, but they enhanced the antibacterial action, observed by a significant reduction in *Enterococcus faecalis* adherent to treated dentin.

Kishenet al. (2008) conducted a study named "An investigation on the antibacterial and antibiofilm efficacy of cationic nanoparticulates for root canal disinfection" The study has highlighted their potential advantage in root canal disinfection.[20] Experiments were performed in two stages. In Stage 1, experiments were conducted to examine the physical properties of three types of nanoparticulates. The antibacterial properties of nanoparticulates alone and nanoparticulates mixed with a zinc oxide-eugenol-based sealer were studied. In Stage 2, the ability of nanoparticulate-treated dentin to prevent bacterial adherence was examined. Zinc oxide nanoparticulates, chitosan nanoparticulates, a mixture of zinc oxide and chitosan nanoparticulates, and zinc oxide nanoparticulates with a multilayered coating of chitosan were tested. This study showed that the incorporation of nanoparticulates did not alter the flow characteristics of the sealer but improved the direct antibacterial property and the ability to leach out an antibacterial component. There was also a significant reduction in the adherence of Enterococcus faecalis to nanoparticulate-treated dentin.

3. Root canal filling materials

Shantiae (2011) conducted the study named "Comparing microleakage in root canals obturated with nanosilver coated gutta-percha to standard gutta-percha by two different methods" in which a silver nanoparticle coating on gutta percha is used to reduce microleakage around the root canal filling material.[21]

4. Implant coatings

Sargeant (2008) conducted an in-vitro study named 'Hybrid bone implants: self-assembly of peptide amphiphile nanofibres within porous titanium', in which Arg-Gly-Asp-Ser nanofibres were incorporated in a nickel titanium alloy and it was found that pre-osteoblasts can survive and proliferate within this compound and can differentiate into osteoblasts to form bone.[22]

Allaker et al. (2010) has shown that a nanohydroxyapatite coating in conjunction with silver nanoparticles can also improve osteoblastic activity and the antibacterial property, and there is a significant reduction in biofilm formation around the implant surface when silver nanoparticles are used.[23]

Applications of nanotechnology in the field of regenerative dentistry

1. Correction of bony defects

E Pinon Segundo (2005) also used nanotechnology in the correction of bony defects and the induction of bone growth.[24] Nanoparticles of hydroxyapatite in various forms are used in bony defect correction. With a reduction in particle size, the surface area increases and makes the material more porous and nanostructured. Nano-bone uses this rule to produce bone grafts.

2. Nanotechnology in guided tissue regeneration

Santoshi Rani et al. (2015) in-vitro study evaluating the Antibacterial Effect of Silver Nanoparticles on Guided Tissue Regeneration Membrane Colonization indicated that the incorporation of silver nanoparticles may be of value when controlling membrane-associated infection.[25] It also suggested that studies with different nanosilver particle sizes should be conducted to further evaluate the beneficial properties of nanosilver against periodontal pathogens.

3

IMPLICATIONS OF NANOTECHNOLOGY

DR. SAVITA HADAKAR

I. Ethical implications

After the research and development phase of any dental or medical nanoproduct, it undergoes extensive preclinical in vitro testing to investigate its mechanical, toxicological and immunological properties. Many agencies such as the US Environmental Protection Agency and the National Institute of Occupational Safety and Health have introduced guide- lines for investigating the risks of nanomaterials.

However, developing a multidisciplinary regulatory framework to assess and control nanotechnology and resolve ethical concerns that fall under the four categories: metaphysical, equity, privacy and security is a constant legislative challenge.[26] Although animal studies provide a reasonable understanding of what to expect when starting a Phase I trial, serious adverse reactions have been recorded when human subjects were exposed to a dose of nanomedicine 500 times less than the recorded toxic limit in 113 animal studies.

Therefore, subjects must understand the level of risk associated with the exposure to novel materials and data and safety monitoring boards must be appointed in every clinical trial, to carefully track and record any adverse side effects early on, pick up inconsistencies in data handling, and ensure the safety and wellbeing of the test subjects.[27]

The unpredictability of nanomaterials creates an ethical dilemma for dentists when faced with a wide range of materials to choose from, some having very long track records supporting their clinical use such as hybrid or microfilled composite resins and others such as the nanofilled composite resins that are appealing in concept and supported by short-term clinical studies. The traditional ethical decision-making process, mainly utilitarian, is unable to keep up with the rapid pace and uncertain future of nano-technological developments. For that reason, a more in depth understanding of the science is required, including a risk/benefit analysis and the ethical considerations throughout the development process.[28] This lead to the proposal of the anticipatory ethics and governance concept, developed to identify and address ethical and societal implications through ethical analysis models when the technology is in its introductory stage, then easily modified and guided towards an ethically acceptable outcome.

A] Ethics in research and development

Before being used in the diagnosis, prevention, or treatment of disease, nanomedicine products must first undergo extensive pre-clinical and clinical testing. Researchers have only just begun to explore the toxicological, pharmacological, and immunological properties of different nanomaterials. The US Environmental Protection Agency, the National Institute of Environmental Health Sciences, the National Science Foundation and the National Institute of Occupational Safety and Health have launched a variety of programmes aimed at studying the risks of nanomaterials. Additionally, the National Cancer Institute has established a laboratory for characterising the in vitro response to ENM that may be used in cancer diagnosis or treatment.[29]

Most researchers point out that safety and risk issues has to be thoroughly understood and taken into consideration if society is to take advantage of the potential benefits of nanotechnology. Assessing the safety of nanomaterials can be a difficult undertaking because they have no common properties other than size (1–100 nm). Since nanomaterials are not a unified class of compounds, each type of material must be assessed on its own terms. Moreover, variations in size and shape can have dramatic and unpredictable effects on the physical and chemical properties of nanomaterials: a substance that is non-toxic at 50 nm may be toxic at 1 nm or vice versa. Because they are heavily dependent on their microenviroment, nanomaterials may change in size or shape inside an organism. A 100 nm particle could disintegrate into 1 nm particles, or 1 nm particles could aggregate into a 100 nm particle. Nanoparticles could behave very differently in an organism than they do in cell culture.

Animal and tissue studies have shown that some types of anthropogenic and naturally occurring nanoscale materials, such as diesel exhaust particles, smoke, and viruses activate pathways that neutralise toxicity, such as oxidative stress, inflammation and innate and adaptive immune responses. Nanomaterials can translocate from the exposure site to other parts of the body. Like some other materials, they can also cross cell membranes and the blood-brain barrier.

Inhaled nanomaterials can enter the capillaries, and once in the circulatory system, they may enter the liver, lymph nodes, spleen and bone marrow. Nanoscale materials may also accumulate in parts of the body and produce adverse effects. The risks associated with exposure to nanoscale materials often varies according to the route of the exposure: a particle that is benign when ingested may be toxic when inhaled.

ENMs, such as fullerenes and C60 carbon shells, may pose more of a danger to human health than naturally occurring nanomaterials because human beings have evolved biological mechanisms for dealing with natural nanomaterials, but not manufactured ones.[30]

Though in vivo animal experiments and ex vivo laboratory analyses can increase our understanding of different nanomaterials, they cannot eliminate all of the uncertainty surrounding the first exposure of a human subject to a particular type of nanomedicine product in a Phase I clinical trial. Ethical guidelines and regulations require that risks to human subjects be reasonable in relation to the potential benefits to the subjects and society and that risks be minimized, wherever possible.[28]

B] Ethics in medical application

A whole different set of issues emerges once a nanomedicine product has moved from the R & D stage and enters the market. A new medical product is often very expensive when it first goes on the market because the manufacturer's patents give it a temporary monopoly. The price of the new product begins to decline when other firms develop competing products and the manufacturer's patents expire. The price continues to decline as generic products enter the market and economies of scale improve the efficiency of production. While it may take a long time for the price of nanomedicine products to decline, due to its complexity and uniqueness, nanomedicine should also become less expensive. In the long run, the intellectual property system promotes human health and reduces health inequalities by providing incentives for investment in biomedical research and development. In the short term, however, intellectual property can exacerbate health inequalities, because economically disadvantaged people may not be able to afford new and expensive medical innovations.[31]

It is likely that nanomedicine products will also be very expensive when they first enter the market, and that nanomedicine may temporarily make health national and international inequalities worse. This problem could be a significant concern in countries that do not have guaranteed health care coverage, such as the US.

To promote national and international justice concerning access to nanomedicine, countries should ensure that intellectual property laws and policies do not give manufacturers excessive control over the market, develop health care financing systems that help poor people receive nanomedicine, participate in international efforts to assist developing nations obtain access to nanomedicine, negotiate fair trade agreements, and encourage companies to institute stratified pricing programmes or other policies that make nanomedicine affordable.[32]

Another ethical issue related to social justice concerns the use of nanomedicine for physical enhancement rather than therapy. The medical enhancement problem is by no means unique to nanomedicine, since almost any new medical technology that can be used to diagnose, prevent, or treat diseases can also be used to enhance the function or appearance of the human body or the human mind.[27] For example, doctors can prescribe anabolic steroids to help patients recover from traumatic injuries, but athletes may also take these drugs to improve their performance. It is likely that nanomedicine will have a major impact on the tension between therapy and enhancement in medicine. Applications of nanotechnology to neurology that help to reduce or replace memory loss could also be used to enhance human memory. Nanomedicine therapies designed to help people with learning disabilities could also allow healthy people to become super-intelligent.

II. Nanotechnology and society

Past experience has shown that the successful introduction of a new technologyrequires careful attention to the interactions between the technology and society. Theseinteractions are bi-directional: on the one hand, technology changes and challenges socialpatterns and, on the other hand, the governance structures and values of the society affectprogress in developing the technology. Nanotechnology is likely to be particularly affectedby these kinds of interactions because of its great promise and the unusually early publicattention it has received. Moreover, it represents a new kind of experiment in packaging arather wide range of fundamental research activities under a single ‘mission-like’ umbrella.Although this gives it more impetus as a field, it sets a higher bar for showing successfulapplications early on and because it links disparate fields, regulatory regimes reasonablefor one kind of nanotechnology development may be inappropriately extended to others.There are a number of lessons to be gleaned from experience with the introduction of othertechnologies, which offer guidance with respect to what pitfalls to avoid and what issues tobe sensitive to as we move forward with the development of nanotechnology applications. The problems encountered by nuclear power point out the dangers of over-promising andthe role the need for the technology plays in ameliorating fears of risk. The public reactionto biomedical engineering and biotechnology highlights, in addition, the cultural factors thatcome into play when technologies raise questions about what is ‘natural’ and what is ‘foreign’ and what conceptions are involved in defining ‘personhood’. In all cases, it hasbeen clear that the main task for those introducing new technologies is building public trust inthe safety of the technologies and the integrity of those introducing it.[33] The advocates ofnanotechnology have already shown that they are generally aware of the need to considerthe public’s reaction, and they have taken the first steps to act on that awareness. We haveto build on those beginnings, and not limit our considerations simply to issues of safety. If wedo so, we have the opportunity to develop a new paradigm for technology introduction, which will serve society well in the future.

III. Health implications

Nanotechnology is rapidly evolving in medical applications: drug delivery, cancer treatment, imaging, disease diagnosis, gene therapy, and also to aid in visual imaging. Nanotechnology is at the cutting edge of rapid health care product development as it has many potential human health benefits, but it is perceived with some apprehension for its potential human health risks.[34] Many fine particles usually considered harmless are likely to acquire unique properties at nano molecular size and could have a toxic effect in human bodies. It is known that this toxicity is dependent on the physical and chemical properties of the particle. Nanomaterials can have different properties from the same material that are not within the nanoscale. The size of the nanoparticle is important when determining the toxicity of it as well as the crystal structure, surface charge and porosity, and the surface area of the agglomeration state.

A] Positive Impact

Nanoparticles are beneficial in many ways in health care; molecular imaging uses nanoparticles which help to detect, quantify and display molecular and cellular changes that happen in vitro and in vivo. Fluorescent biological probes using organic dyes are used conventionally in biology because of their inert qualities and their ability to interact without loss of sensitivity in a variety of cellular reactions. In vivo, nanoparticles can be used as probes by attaching them to the molecules of proteins, antibodies and nucleic acids. These nanoparticles can then be used as tools for displaying and quantifying molecular reactions inside the body. They have high photostability, high levels of brightness and absorption coefficients across a broad spectral range. Site-specific targeted drug delivery using nanoparticles is more effective for improved bioavailability, minimal side effects and decreased toxicity to other organs and is less costly. An exciting potential use of nanoparticles in cancer treatments is the exploration of tumour-specific thermal scalpels to heat and burn tumours. By using near infrared-absorbing polyethylene-coated gold nanoshells of 130 nm, they can be used to inhibit the growth of a tumour.[35] Gold and silver nanoparticles have strong antifungal, antibacterial and anti-inflammatory properties and are used in anti-wrinkle creams, deodorants and burn medications. They are inert, highly stable, biocompatible and non-cytotoxic. Scientists have come across many health benefits of nanotechnology. But do we know whether these nanoparticles can also have an adverse effect on our health, depending on the exposure and quantity?

B] Negative Impact

As discussed earlier, the toxicity of nanoparticles depends on their surface properties, coating, structure, size and ability to aggregate. If nanoparticles have poor solubility they can cause cancer. This is because the nanoparticles have a greater surface area to volume ratio which increases the chemical and biological reactivity. The nanoparticles can enter the body through many routes; dermally, by ingestion, inhalation, injection or by implantation. Nanoparticles enter dermally when they are present in skincare products, hair products or lip balms, including sunscreens and anti-wrinkle cream. Cosmetic products need no clinical trials but have the maximum number of products with nanoparticles. The nanoparticles in these products have been reported to cause erythema, and the cobalt and chromium nanoparticles cross the skin barrier and damage fibroblasts. Many mechanisms have been proposed to explain the adverse effects which may lead to cardiopulmonary morbidity and mortality in populations exposed to nanoparticles. Nanoparticles can stimulate the neurons in the lungs, affecting the central nervous system and cardiovascular autonomic function. When they gain access to the circulation, they can trigger an acute inflammatory reaction, as these particles are recognised and identified by the immune system of the body as 'invader' particles.[36] The immune system starts releasing cytokines which is a chemical substance usually released whenever the body is exposed to foreign materials. These particles cause a reaction in the lungs the same as that of any pollutant or inflammatory substances, sometimes also affecting the reactive oxygen species (ROS). In extreme situations this can trigger cardiac events.

C] Remedial Solution

Every scientist using nanoparticles, or being exposed to them, should use protection such as a mask, gloves etc. while working with the nanomaterials. They should also be careful about the disposal of these materials once experiments are completed, to ensure that these harmful particles do not enter the environment and exacerbate the new classification of pollution, which is nano-pollution. The WHO has already listed a series of health implications on exposure to nanoparticles. But how large is the risk and what should the regulations and policies be, that have not yet been formulated.[34] The current evidence is not conclusive. Different models and frameworks for risk estimation are being developed to organise the available data on the health effects of nanomaterials and methods to incorporate them into a policy. Many countries are yet to have regulation in place regarding usage of nanoproducts. It is important to use regulatory mechanisms and laws during the production and usage of nanomaterials.

4

DEVELOPMENT OF NANOTECHNOLOGY

DR. SWAPNIL TAUR

The ‘Nanotechnology’ term is derived from the Greek word ‘nanos’, which means dwarf. The Nobel Prize winning physicist, Richard P. Feynman, during his 1959 ‘Plenty of Room at the Bottom’ speech to the American Physical Society, had first projected this dimension of discoveries at a billionth metre scale.[37] The term nanotechnology was introduced by Norio Taniguchi in 1974, when he referred to a ‘production technique to get extra high accuracy and ultra-fine dimensions’.[38] Later, in 1986, K. Eric Drexler contributed to its development by introducing the concept of molecular nanotechnology in his 1986 publication *Engines of creation: the coming era of nanotechnology*.[39]

Applications in the field started in the 1980s with the invention of the scanning tunnelling microscopes and the discovery of carbon nanotubes and fullerenes. However, major initiatives began at the beginning of this century, thus ushering in the era of nanotechnology. According to the National Nanotechnology Initiative, a United States government research and development programme, nanotechnology involves the, ‘…research and technological development at atomic, molecular, or macromolecular levels, in the length scale of approximately 1-100 nanometer (nm) range, with creation and use of structures, devices, and systems that have novel properties and functions as a result of their small and/or intermediate size; and ability to control or manipulate matter on the atomic scale’.[40] Nanotechnology involves the development of materials, devices and systems exhibiting properties that are different from those found on a larger scale. In the nanodimension range of 1-100 nm, the lower limit is marked by the size of a hydrogen atom (0.25 nm) and the upper limit commences from a size where phenomena different from larger structures start appearing. Figure no. 01 is giving a size comparison of a nanoparticle with other larger-sized materials.[41] In other words, if a child’s marble is