Relevance of nanotechnology to Africa: Synthesis, Applications and Safety

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Abstract

In this chapter, two nanotechnology-based applications relevant to Africa in promoting sustainability and achievement of the Millennium Development Goals (MDGs) are presented. The applications comprise the provision of therapeutic treatment of diseases (HIV/AIDS and malaria) and the treatment of contaminated water through purification, remediation and disinfection process to promote access to clean water to millions of African inhabitants without clean drinking water. Extensive examination of the available scientific literature suggests that nanotechnology potentially can improve the provision of health and water services in the African continent. Whilst the authors agree these benefits are of great relevance to the continent, the chapter gives insights on the concerns related to potential risks posed by nanotechnology-based products both to humans and other ecological systems. In addition, the chapter seeks to outline chemistry underpinning the development of nanotechnology and its relevance in achieving sustainable development within the context of developmental challenges in Africa. Finally, as the future socioeconomic status will be mostly defined by nanotechnology capabilities, Africa should be alert to these changes and take advantage, particularly, at this early development phase of nanotechnology development.

Introduction

What is Nanotechnology?

Nanotechnology is the science of manipulating materials at very small scales, i.e. at the atomic and molecular levels. Nanotechnology allows for the design, synthesis, and control at the length scale range of 1 – 100 nm. This is about ten thousand times smaller than the width of human hair and is in the range of the size of a large protein structure. Nanotechnology is a broad interdisciplinary area of research, development and industrial activity in which the unifying characteristic is one of size.

The prospects of research in nanotechnology also known as the science of the ultra small, was first made known by Nobel Prize winning physicist Richard Feynman in 1959. Since then the concept of nanotechnology surfaced with the idea that atoms could be used to build structures, with absolute control over properties and functions. While materials in the micrometer scale often exhibit physical properties the same as that of the bulk form, it is interesting to note that materials in the nanometer scale may exhibit physicochemical properties uniquely different from their counterpart bulk materials of the same chemical composition. For example, bulk semiconductors become insulators when the characteristic dimension is sufficiently small (within the nanometer region). The underlying difference is size dependency with the effect becoming more prominent when the particles are 100 nm or less in diameter.

As the particle size of materials decreases to nano level a change in physical phenomena is inevitable. Quantum size effect takes precedence as the electronic properties of solids are altered with this reduction in particle size to the nanoscale– accompanied by dramatic increase in the number of atoms at the surface of the material. This results in change in numerous physical properties such as mechanical, electrical, optical, surface properties. Nanoparticles, due to their small size, have a high surface-to-volume ratio and this leads to improved mechanical, thermal and catalytic properties.

Nanotechnology: a chemistry perspective

Synthesis of materials at nanometre scale is now a routine practice and an active field of research. Materials with one or more dimensions below 100 nanometres, the normal rules of physics and chemistry no longer apply and many materials start to exhibit novel and unique properties. They may have large surface area, become stronger, more conductive, and with improved optical properties amongst others. As such nanomaterials are also defined in terms of novelty and uniqueness of properties they possess as a result of small dimensions.

In Africa, nanotechnology has already been recognized as an important tool for industrial development, and a means to improve the lives of ordinary people through more efficient health care services, safe drinking water and low cost clean energy production.

Although the advanced concept of nanotechnology is still novel, research on the nanometer scale is not new at all. For example biological systems and the engineering of many materials such as colloidal dispersions and metallic quantum dots have been extensively studied at a nanometer level. Catalysis is also known to be the milestone field when it comes to the use of nanoparticles. This occurred long before the inception of the field of nanotechnology. The high surface area of catalyst particles means that the surface effects are far more significant than in the bulk substance. Nanotechnology comprises of molecules, atoms and quantum dots - and is dominated by surface effects such as Van der Waals forces of attraction, hydrogen bonding, electronic charge, ionic bonding, covalent bonding, etc. The vastly increased ratio of surface area to volume gives new possibilities to surface-based sciences such as catalysis. To illustrate the contribution of chemistry to the development of Africa, in the following sections, a few examples of nanomaterials chemistry is presented.

Inorganic Nanoparticles

Insoluble inorganic nanoparticles comprise of pure metals, metal oxides or various inorganic products and alloys. In the following, examples of each type are presented for illustrative purposes.

Metal-based nanoparticles

Gold nanoparticles (nAu)

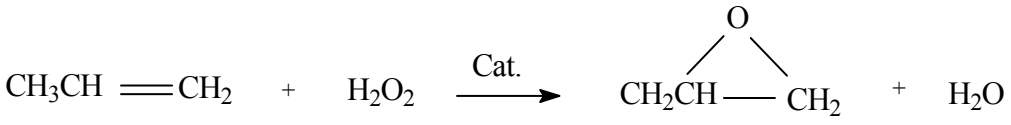
Colloidal gold has increasingly received considerable attention since they hold promise in technological advancement and development. For example, due to their nanosized dimensions gold colloids exhibit interesting optical properties (Puddephatt, 1978). Depending on the particle size, shape, and agglomeration gold colloids can be red, violet or blue. Gold colloids also find applications in areas of histochemistry and cytochemistry where they are used as electron-dense labeling agents (Hyatt & Eaton, 1993). Moreover, due to high thermal and electrical conductivity they also find application in electronics (Hayat, 1989).

Gold is also widely used in biocatalysis and catalysis. Nano gold has been widely used to construct biosensors due to its excellent ability to immobilize biomolecules such as proteins, enzymes and antibodies whilst maintain the biocatalytic activities of those biomolecules (Alivisatos, 1996; Mckenzie & Marken, 2003). Supported gold catalysts provides a high catalytic activity in numerous reactions such as the reduction of nitrogen oxide (equation 1), low temperature for the oxidation of CO (equation 2) and the epoxidation of propene (equation 3) (Haruta, 1997). The high catalytic activity of gold is not uniquely strange as bulk gold is quite inert. Reactive molecules such as CO and H_2 do not adsorb on the surface of gold. However, this behaviour dramatically changes when gold is highly dispersed as nanosized particles on certain metal oxides including TiO_2 (Haruta *et al.*, 1993; Wang & Koel, 1998).

The success to achieve highly dispersed nAu is underpinned by method and conditions of synthesis. Typically colloidal gold nanoparticles are prepared by treatment of $HAuCl_4$ with $NaBH_4$ or with Ag (equation 4). Furthermore, for catalysis purposes incipient wetness impregnation is unsuitable to produce well dispersed gold catalysts. In order to obtain high activity the catalyst has to be prepared via co-precipitation or deposition precipitation (Okumura *et al.*, 1997).

$$4NO + 4NH_3 + O_2 \xrightarrow{\text{Cat}} 4N_2 + 6H_2O \qquad (1)$$

$$CO + 1/2O_2 \xrightarrow{\text{Cat.}} CO_2 \quad (2)$$



(3)

$$3Ag\,(s) + HAuCl_4\,(aq) \longrightarrow Au\,(s) + 3AgCl\,(aq) + HCl\,(aq) \quad (4)$$

Silver nanoparticles (nAg)

nAg are synthesised either using traditional or non-traditional methods which have recently been reviewed by Evanoff and Chumanov (Evanoff & Chumanov, 2005). Silver nanoparticles are synthesised either by using traditional Creighton methods where the $AgNO_3$ is reduced with $NaBH_4$**,** or through non-traditional methods where Ag particle synthesis is achieved among through numerous methodologies including photoreduction of Ag ions (Abid *et al.*, 2002) or electrolysis of an Ag salt solution (Zhu *et al.*, 2000). Similar to nAu, nAg can also be synthesised in different shapes (Sun & Xia, 2002; Cobley *et al.*, 2009).

Nanoscale Zero-Valent Iron (nZVI)

nZVI can be created in a variety of different ways such as the reduction and precipitation of ZVI from an aqueous solution using sodium borohydride. nZVI also can be produced by hydrogen reduction of iron oxides or hydroxides (Macé *et al.*, 2006). .nZVI may react with water and oxygen where Fe0 becomes oxidized to ferrous (Fe^{2+}) ions where the electrons released will become available to reduce other compounds (equations 5 and 6) (Zhang & Elliott, 2006).

$$2Fe^0{}_{(s)} + 4H^+{}_{(aq)} + O_{2(aq)} \rightarrow 2Fe^{2+}{}_{(aq)} + 2H_2O_{(l)} \quad (5)$$

$$Fe^0{}_{(s)} + 2H_2O_{(aq)} \rightarrow Fe^{2+}{}_{(aq)} + H_{2(g)} + 2OH^-{}_{(aq)} \quad (6)$$

nZVI is highly reducing and generates reactive oxygen species (ROS) through Fenton chemistry (Zhang, 2003).

Metal oxide-based nanoparticles

Titanium dioxide nanoparticles ($nTiO_2$)

Because of its availability and relatively low cost of production, $nTiO_2$ has been widely used in catalysis as a catalyst or support. Moreover, its low surface area is an important limitation for catalytic applications (Wei *et al.*, 1990; Weibel *et al.*, 2006). In order to alleviate this problem scientists have developed a variety of new synthesis procedures to prepare $nTiO_2$ with a higher specific surface area. Nevertheless, for many other applications, titanium dioxide can also be modified by insertion of metal ions to enhance both performance and activity (Pajonk, 1991; Reluert *et al.*, 1998).

Titanium dioxide is known to exist in three main crystallographic structures, namely; anatase, rutile and brookite. Among the three polymorphs of titanium dioxide, anatase is known to have a higher photoactivity than both rutile and brookite (Fox & Dulay, 1993; Sopyan *et al.*, 1998). It is therefore advantageous to produce the anatase powder with a high degree of crystallinity and high surface area (or small grain size) to enhance the photocatalytic activity (Zhang *et al.*, 1998).

There are various methods available for the production of small $nTiO_2$ but the sol-gel method has been widely used since it is deemed relatively inexpensive. Unfortunately, the sol-gel derived material is amorphous in nature and often requires a further treatment to induce crystallization (Wang & Ying, 1999). Elevated treatment temperatures (higher than 350 ^{o}C) are often necessary to expedite the transition from the amorphous material to the crystalline anatase phase but such high temperatures result in increased size of the nanoparticles and subsequently a decrease in the surface area (Huang *et al.*, 2000; Liu *et al.*, 2002a).

Zinc oxide nanoparticles (nZnO)

ZnO is a very useful material and finds versatile applications in technologies such as gas sensors, UV light emitters, varistors, pigments, and catalysts just to mention a few. It also has shown potential applications in UV blocking in cosmetics and suncreens, optoelectronics and an excellent candidate for blue to UV lasing (Mahmood *et al.*, 1995; Look, 2001). Zinc oxide is a semiconductor material with wide direct band gap energy of 3.37 eV and a large exciton binding energy (60 meV) which emits blue light in bulk form because of the bombardment with electron beam at cryogenic temperature (Hvam, 1973; Klingshirn, 1975). However, when particles are reduced to nanoscale level the material starts to emit even at low temperature with low threshold.

The ever-growing interest in is largely driven by chemical stability and modest production costs. Though the nanoparticles may provide improved specific microstructural, surface and chemical properties further modification by introducing metal ions may alter both the electrical and optical properties of the material (Caillaud *et al.*, 1992; Musić *et al.*, 2003). On the other hand, several methods of synthesizing ZnO nanocrystals have been developed including thermal transport and condensation template and surfactant assisted liquid methods (Wang & Li, 2002; Chu *et al.*, 2007).

Although these methods are relatively inexpensive and generate products that are pure and homogeneous but are limited in a number of ways. For example, the removal of the homogeneously mixed template is always a challenging task (Wang & Li, 2002). However, hydrothermal synthesis has proven to be a facile method for the synthesis of nZnO. The use of microwave assisted hydrothermal is also an alternative option that offers many advantages such as low cost, short reaction time, high purity and large scale production. Studies have shown that the morphology of nanoparticles of nZnO may be influenced by factors such as synthesis method and temperature (Sun & Xia, 2002). The hydrothermal synthesis of nZnO using hydrothermal synthesis is carried out in the presence of a strong alkaline solution such as NaOH or KOH. The overall reaction is summarized in equation 7.

$$[Zn(OH)_4]^{-2} \xrightarrow{\text{heat}} ZnO + H_2O + 2OH^- \quad (7)$$

Organic nanoparticles

Biodegradable polymer nanoparticles

As in the case of inorganic nanoparticles, insoluble organic nanoparticles consist of various organic substances - often insoluble polymers. Biodegradable polymer nanoparticles are used for drug delivery with diffusion-controlled, delayed dissolution, or drug solution flow control mechanisms (Uhrich *et al.*, 1999). Polymers used for controlled drug release include the well-known poly(esters) and several examples include polylactic acid (PLA), polyglycolic acid (PGA), or PLGA, a copolymer of PLA and PGA; poly(ortho esters), such as 3,9-diethylidene-2,4,8,10-tetraoxaspiro[5,5]undecane (DETOSU]-based poly(ortho esters); poly(anhidrides) such as sebacic acid (SA), *p*-(carboxyphenoxy)propane (CPP) and *p*(carboxyphenoxy)hexane (CPH) based poly(anhydrides); poly(amides) or poly(amino acids) such as poly(lactic acid-*co*-lysine) (PLAL); and finally phosphorous-containing polymers.

Polymeric nanoparticle drug delivery systems have been shown to encapsulate a variety of therapeutic compounds (Finkelstein *et al.*, 2003; Koushik *et al.*, 2004; Destache *et al.*, 2009). For example, biodegradable polymer nanoparticles, consisting of polylactic acid (PLA), polyglycolic acid (PGA), or a copolymer of PLA and PGA (Finkelstein *et al.*, 2003; Destache *et al.*, 2009), have been investigated for the delivery of proteins and genes (Panyam *et al.*, 2003; Panyam & Labhasetwar, 2003), vaccines (Nugent *et al.*, 1998) and anticancer drugs (Brannon-Peppas & Blanchette, 2004). However, due to copolymer crystallization, aggregation, low biodegradation rate or poor flexibility, the application of polymer nanoparticles is limited. In order to prevent the aggregation of PLGA particles, anionic, cationic, non-ionic and zwittterionic (amphoteric) polymer stabilizers are often used (Stevanovic *et al.*, 2009).

The highly branched and symmetrical molecules known as dendrimers are the most recently recognized members of the polymer family because of their unique branched topologies which confer them with properties that differ substantially from those of counterpart linear polymers.

Dendrimers were first synthesized by Vögtle and colleagues in 1978 (Buhleier *et al.*, 1978). They are 3-dimensional globular monodisperse highly branched polymers prepared in a series of repetitive reactions from simple branched monomer units emitted from a central core with an exterior corrugated surfacing whose size and shape can be precisely controlled. Dendrimers are fabricated from monomers using either convergent or divergent step-growth polymerization. Dendrimer's unique architecture enhances their ability to exhibit high functional structures (Zeng & Zimmerman, 1997; Lee *et al.*, 2005). Subsequently, a wide range of dendrimers of different structural classes are synthesized using divergent (built from the central core to the periphery), or convergent (built from the periphery toward the central core) strategies – using repeat units ranging from pure hydrocarbons to peptides, or coordination compounds.

The well-defined structure, monodispersity of size, surface functionalization capability, and stability are properties of dendrimers that make them attractive drug carrier candidates. Drug molecules can be incorporated into dendrimers via either complexation or encapsulation. Dendrimers are being investigated for both drug and gene delivery (Hussain *et al.*, 2004), for instance, as carriers for penicillin (Yang & Lopina, 2003), and in anticancer therapy (Quintana *et al.*, 2002). Other dendrimers applications include catalysis (Albrecht *et al.*, 2000; Kleij *et al.*, 2000), and molecular encapsulation for light harvesting (Stewart & Fox, 1996; Hofkens *et al.*, 2000).

Nanotubes

Carbon-based nanotubes

Carbon nanotubes (CNT)

The discovery of carbon nanotubes has led to the dawn of discoveries of nanostructured materials and technologies (de Heer *et al.*, 1997). The main drive has been their unique structure and properties (Tans *et al.*, 1997). CNTs have versatile applications in areas such as electronic devices, tools in nanotechnology, hydrogen storage, water purification, etc. (Dai *et al.*, 1996). There are two forms of manufactured carbon nanotubes - the single-walled carbon nanotubes

(SWCNT) and multi-walled carbon nanotubes (MWCNT). The SWCNT is made up of a single layer of graphene sheet rolled-up as cylindrical shapes. The rolling up of these graphene layer(s) results in unique electronic structure. SWCNT has an internal diameter of approximately 1 nm and a length of several microns. On the other hand, MWCNTs are made up of two or more concentric layers with various lengths and diameters (Gao, 2004).

Various methods have been utilized to generate carbon nanotubes and include arc evaporation, laser ablation, chemical vapour deposition (CVD), etc. (Endo *et al.*, 1993). The synthetic yields of SWCNT is often very low but can be improved by adding cobalt or other transition metals such as nickel, iron and molybdenum. In all the synthetic routes, the generation of carbon species (atoms) involves heating the precursor at 600 to 1200 ^{o}C under inert ambience and the use of catalytic metal (Rinzler *et al.*, 1998). Both SWCNT and MWCNT contain a proportion of amorphous carbon (non-tubular) and metal residual as impurities. Post treatment of these materials is, thus, important to remove all contaminants. Post treatment procedures include gas phase, liquid phase and intercalation technique. It is important to preserve the aspect ratio of tubes during the purification process (post treatment) in order to retain the inherent unique properties of the materials. Some of these properties include mechanical, thermal, photochemical and electrical properties which are of industrial use (Amelinckx *et al.*, 1994; Loiseau & Willaime, 2000).

Metal oxide-based nanotubes

Titanium dioxide Nanotubes

Nanotechnology has made the synthesis of nanotubular materials possible, with carbon nanotubes at the forefront. Nanotubes of many semi-conducting metal oxides such as TiO_2 have also attracted much attention (Hoyer, 1996). Due to the outstanding physical and chemical properties of the novel TiO_2 nanotubes many applications have been anticipated. The morphological feature and high surface area of the tubes have offered TiO_2 materials a variety of application in catalysis. Nanotubular TiO_2 materials are currently used as a support in areas such as catalysis (Liu *et al.*, 2002c). They have also been used as a photocatalyst in the treatment of

water and due to the optical properties of the material, nanotubes of TiO_2 have been incorporated into flat panels for improved display (Wang *et al.*, 2002).

The ever-growing interest in titania derived nanotubes is driven mainly by the large surface area, chemical stability, and the modest production costs of the tubular materials (Ivanovskaya *et al.*, 2003). Conventionally the sol–gel method has been widely used to synthesize TiO_2 derived nanotubes using templates such as organogels or porous anodic alumina (Kasuga *et al.*, 1997; Jung *et al.*, 2002). These methods are relatively inexpensive and offer numerous advantages since the final products are pure and homogeneous (Imai *et al.*, 1999; Liu *et al.*, 2002b). However, the removal of the homogeneously mixed template is invariably a challenging task (Mahata *et al.*, 2001).

Hydrothermal synthesis has increasingly been used to generate TiO_2 nanotubes. The advantages of using hydrothermal synthesis include the utilization of relatively fewer chemical reactants. The products obtained have high levels of purity, and the use of water as solvent renders the process environmentally friendly.

Recently there has been a growing effort to utilize microwave heating in search for methods that allow the production of nanomaterials with well controlled properties. Microwave heating is particularly useful for reactions carried out under elevated pressures, because of contactless delivery of energy to the reading fluids, high energy density possible, and short heating times leading to nanoparticles weakly agglomerated, with high crystallinity and narrow grain size distribution.

Catalysis and nanoparticles in water purification and other applications

The science of catalysis is driven by technology, as it has been from the beginning of studies on catalysts. The primary objective in catalysis research is to design catalysts that can achieve perfect selectivity and desirable activity. It is commonly acceptable that selectivity is much more difficult to achieve and control. Thus, a reaction that yields a perfect selectivity would not

generate spin off products thereby reducing energy and process requirements for separation and purification (Kirk-Othmer, 1993).

Many of the products that support our everyday lives - fuels, fertilizers, construction materials, medicines and artificial fibres, to name but a few – involve heterogeneous catalytic processes at one or several stages in their manufacture. By heterogeneous catalysis we mean that the catalyst has a distinct and separate phase from that of the reactants so that the catalytic reaction takes place at a boundary, or interface, between phases (Christoffel, 1989). In most cases of practical interest the catalyst is a solid while the reactants are in the fluid phase (gas, liquid or solution), so that under these conditions the catalytic reaction takes place at the surface of the solid. The subject of heterogeneous catalysis is very broad and embraces a wide field of physical, chemical and engineering sciences (Corma, 1995).

A good catalyst should have active sites where chemical transformation occurs to enhance bond formation and breaking. The interaction between the surface of the catalyst and the reactant molecules is crucial as it affects the adsorption and desorption of the reacting species. In the past two decades the use of homogeneous catalysts has dramatically declined due to the difficulties associated with the separation of reaction products and costs thereof. Solid catalysts, on the other hand, are environmentally benign and more compatible with increasingly demanding environmental requirements (Corma, 1995; Ardizzone *et al.*, 1999).

Due to their large surface area, nanoparticles may therefore provide higher catalytic activity. For example, synthesis of titania nanostructures and their application as catalyst supports for hydrogenation and oxidation reactions has recently been presented (Sikhwivhilu *et al.*, 2008) and the use of gold-titania in active CO oxidation was also investigated (Boyd *et al.*, 2005).

*Nanotechnology Applications: the African cont*ext

For the nanotechnology applications to be relevant and sustainable in the Africa context, the technology should offer social and economic utility values. In this section, we argue that the nanotechnology can enhance sustainability within the context of solving the African continent

challenges given it can provide novel solutions to societal needs that accelerate the achievement of the millennium development goals (MDGs), and secondly, proactively support socio-economic developmental challenges. Salamanca-Buentello et al (Salamanca-Buentello *et al.*, 2005) ranked the top ten applications of nanotechnology that can support sustainable development issues in the developing world including Africa. Similarly, the United Nations Environment Development (UNEP, 2007) report suggested nanotechnology has the potential to contribute to the target set for achieving the UN MDGs specifically in the areas of water, energy, health, and the environment. Given the MDGs were set in an attempt to lift the livelihoods of millions of people in the developing countries – including Africa, these areas of need appear as the most appropriate areas for the nanotechnology applications in a resources-limited region as Africa.

Conversely, this case is strengthened by the well known environmental, economic, and social impacts of poor water supply and sanitation (Montgomery & Elimelech, 2007) (as well as the health and welfare of people – especially the vulnerable groups like the elderly, children, poor, and those with compromised health systems (Eshelby, 2007)). It is in this context that, several African countries have initiated activities on nanotechnology research and development (e.g. South Africa, Egypt, and Botswana), or have expressed interest in the technology (e.g. Tanzania, Ghana, Senegal, Kenya, Swaziland, and Zimbabwe) (Maclurcan, 2005). Over the last five years, the authors contend that the situation is likely to have changed, however, little has been published to expound on the account of the intended uses of nanotechnology in most Sub-Saharan countries except South Africa.

Therefore, using the South Africa National Nanotechnology Strategy (NNS) (DST, 2005) and the Ten-Year Research Plan (DST, 2010) as guiding pillars of addressing socially-related development needs using nanotechnology – the application fields include health, water, and energy. Conversely, the industrial-based application includes the beneficiation of minerals as well as supporting advanced materials manufacturing, and chemical and bio-processing (DST, 2005; DST, 2010). As the focus of the chapter is to examine the contribution of nanotechnology to support sustainable development in the broader Africa context – only the social-related applications are summarized.

Nanotechnology: water-related applications

Nanotechnology is a suitable platform to offer sustainable solutions to address challenges related to; water scarcity, increasing quantities of portable water, and improving clean water supply for domestic and industrial uses in the developing countries – including Africa (Hillie & Hlophe, 2007). For example, Hillie et al (Hillie *et al.*, 2006) report identified specific opportunities associated with nanotechnology applications especially those with potential utility value in the developing world. The authors identified the use of nanofiltration as a suitable technology for the treatment of water in developing countries.

In this section, several examples are presented to illustrate the contribution of nanotechnology in enhancing water quality and quantity particularly in the rural dwelling settings. Broadly, nanotechnology finds potential application in water purification through water treatment, bioremediation, purification, and disinfection processes. Detailed and excellent review of nanotechnology applications and potential long-term opportunities in water treatment has been presented by Cloete and co-workers (Theron *et al.*, 2008).

Water purification

Conventionally, numerous and diverse water treatment technologies have been developed over the years to purify water including sedimentation, activated carbon, coagulation-flocculation, adsorptive filtration using ion exchange resins, and biological processes. However, many of these processes have shown serious limitations in removing dissolved salts as well as soluble inorganic (e.g. heavy metal ions) and organic pollutants from contaminated water. Baker (Baker, 2004) summarized the fundamental principles of membrane technology and their applications in water and wastewater treatment, desalination as well as water reclamation. Examples of membranes comprise of microfiltration (MF), ultrafiltration (UF), and nanofiltration (NF), and reverse osmosis (RO).

Several nanotechnologies have been investigated for potential applications in water purification systems. For example, Srivastava et al. (Srivastava *et al.*, 2004) presented results on the

production of nanostructured membranes – carbon nanotubes filters – characterised by ease of manufacturing them and controlling their cylindrical geometry – comprising of radially aligned carbon nanotubes. These carbon nanotubes-based filters were shown to be effective in removing 25 nm-sized polio virues (*Poliovirus sabin 1*) and bacterial pathogens (*Escherichia coli* and *Staphylococus aureus*) from contaminated water. The filters performance was found higher in comparison to that of the conventional membranes due to their high thermal and mechanical stability, large surface area, reusability (achievable through ultrasonication or autoclaving), high influx, and relatively low production cost. On the other hand, branched dendrimers supported in polymers comprising of a central core, repeating units, and terminal functional groups were also used (Tully & Frechet, 2001). There are mainly two types of dendrimers; hyperbranched polymers (Gao & Yan, 2004) and cyclodextrins (Del Valle, 2004). The diversity of these nanomaterials in water purification is achieved through functionalization, for example, cyclodextrin polyurethanes copolymerised with functionalized multiwalled carbon nanotubes as adsorbents exhibited capability to remove organic pollutants present at nanograms per litre ($ng \cdot \ell^{-1}$) or lower in water (Mamba *et al.*, 2007; Salipira *et al.*, 2008).

Other studies have shown potential applications of cyclodedrins for the removal of pesticides (Sawicki & Mercier, 2006) and organic pollutants from contaminated water (Arkas *et al.*, 2006). Removal of organic pollutants is enhanced using $nTiO_2$ porous ceramic filters impregnated with an alkylated poly(propylene imine) dendrimer, poly(ethylene imine) hyperbranched polymer or *β*-cyclodextrin, thus resulting in hybrid organic/inorganic filter modules. The modules are characterised by high mechanical strength and high surface area. The results of testing the filters showed the polycyclic aromatic hydrocarbons (PAHs) pollutants removal exceeded 95% whereas those of trihalogen methanes (THMs), monoaromatic hydrocarbons (benzene, toluene, xylene) and pesticides (simazine)) were also removed efficiently above 80%. Finally, other studies have demonstrated the effectiveness of using metal-based nanoparticles such as silver and gold to remove pesticides (e.g. endosulfan, malathion and clorpyrifos) (Nair & Pradeep, 2003). The findings suggested the reaction products were environmentally benign, no by-products were generated, and exhibited high selectivity of nanoparticles in treating the targeted pollutants in comparison to the counterpart bulk form of noble metals, and the capability to target a large range of pesticides such as halocarbons (e.g., benzyl chloride, chloroform, and bromoform),

organochlorine pesticides (e.g., endosulfan) and organophosphorus pesticides (e.g., chlorpyrifos, malathion). Using sensitive instrumentation, it was established that all such organics underwent complete mineralization at low concentrations (Predeep, 2009).

Water remediation

In Africa, there are expansive contaminated water and soil environments due to large industrial, mining, agricultural, and poor waste disposal activities as well as leakages from petrochemical storage tanks. The most dominant pollutants include the toxic heavy metals (e.g. arsenic, mercury, cadmium, lead, etc), toxic effluents such as the acid mine drainage (ADM), pesticides and organic pollutants. Most pollutants exhibit high biopersistence, bioaccumulation, and long half-lives (not easily biodegradable) in the environment. As a result, they cause diverse adverse effects to humans such as cancer, liver damage, and deformations in babies. In addition, they disrupt the environmental ecosystems through distortion of community populations to plants, invertebrates, and vertebrates. However, majority of the traditional technologies like solvent extraction, activated carbon adsorption, and common chemical oxidation, whilst effective, have serious limitations as they are costly, laborious, and time-consuming (Schwarzenbach *et al.*, 2006). In addition, whereas the biological degradation techniques are environmentally friendly and cost-effective, they are time-consuming (Ahluwalia & Goyal, 2007).

It is within the constraints of the current technologies such as in ability to remove the toxic contaminants from the environment to safe levels, long lead time requirements, and high costs (Savage & Diallo, 2005) that motivated research efforts in search of alternative efficient techniques of cleaning contaminated regions. The use of nanomaterials has become one active area of research efforts of remediating contaminated soils and underground waters due to their strong reduction effect in transforming toxic into less or non-toxic pollutants. This is enhanced by their large surface area, high reactivity, and sequestration properties (Tratnyek & Johnson, 2006). At present, a large number of nanoparticles and nanomaterials have been researched as potential candidates for remediating industrial effluents, groundwater, surface water, and drinking water, and recently have been comprehensively reviewed (Theron *et al.*, 2008).

For illustrative purposes, the use of zero-valent iron nanoparticles (nZVI) – which is the most studied metallic nanoparticle for the environmental remediation (Wang & Zhang, 1997), is briefly discussed. Findings show that nZVI are very effective for the transformation and detoxification of a wide variety of common environmental contaminants like chlorinated organic solvents, organochlorine pesticides, and PCBs (Zhang, 2003). In addition, nZVI are effective in reducing other contaminants such as nitrate (Liou *et al.*, 2006), perchlorate (Cao *et al.*, 2005), chromate (Ponder *et al.*, 2000), arsenite (Kanel *et al.*, 2005) to benign by-products. And finally, nZVI has shown great potential in removing heavy metals (e.g. lead, copper, arsenic, nickel, etc) from solution or dramatically reducing their reactivity (Ponder *et al.*, 2000; Kanel *et al.*, 2005; Li & Zhang, 2006).

Keum and Li (Keum & Li, 2004) showed the effectiveness of the nZVI in remediating pesticides through the reduction of debromination of polybrominated diphenyl ethers (PBDEs) where over a 40 days period 92% of BDE congener 209 was transformed into lower bromo congeners. In addition, under five days, hexa- to heptabromo BDEs were found the most abundant products, but the tetra- to pentabromo congeners were dominant after 2 weeks. More importantly, no oxidation products were detected in all these experiments. The results suggest that a stepwise debromination from n-bromo to (n-1)-bromodiphenyl ethers was the dominant reaction in all congeners. Debromination of PBDEs by zero-valent iron has high potential values for remediation of PBDEs in the environment (Zhang & Fang, 2010).The potential of nZVI for remediating underground water has reported (Elliot & Zhang, 2001). Elliot and Zhang (2001) reported that trichloroethene (TCE) were reduced up to 96% after injecting 1.7 kg of nZVI into the underground water. Despite the remarkable results reported to date on the use of nZVI for remediation in groundwater, findings in soil environments are lacking or limited. Therefore, in order to improve the large scale application of the nZVI for remediation applications, several challenges merit redress. These include avoiding or eliminating the aggregation of nZVI several using stabilizers such as water-soluble starch (He & Zhao, 2005), hydrophilic carbon or polyacrylic acids (Schrick *et al.*, 2004), sodium carboxymethyl cellulose (CMC) (He *et al.*, 2007), and polymers (Saleh *et al.*, 2007).

Water disinfection

The current conventional water disinfection techniques exhibit numerous limitations. This has formed the basis for active research efforts towards the development of alternative technologies including the application of nanotechnology in water disinfection have been initiated over for the last few years. The proposed technologies are likely to generate great appeal to the developing countries because of their low cost, do not require complex technological support (simple to apply), produces no harmful by-products, and can support decentralized or point-of-use water treatment and reuse systems. In this chapter, few examples are presented to illustrate the utility of nanotechnology for water disinfection (for detailed review see (Li *et al.*, 2008; Theron *et al.*, 2008).

Nanoparticles have been shown to possess strong antimicrobial properties (e.g. $nTiO_2$, nZnO, nAg and fullerol) through diverse mechanisms including photocatalytic production of reactive oxygen species that damage cell components and viruses ability to compromise the bacterial cell envelope (e.g. peptides, chitosan, carboxyfullerene, CNTs, nZnO, nAg), interruption of energy transduction (e.g. nAg and aqueous nC60), and the inhibition of enzymatic activity and DNA synthesis (e.g. chitosan) (Li *et al.*, 2008). The nanoscale-based disinfectants have proven to possess similar or superior antibacterial activities in comparison to the conventional chemical disinfectants. For instance, $nTiO_2$ on a thin film in a UV reactor have showed higher bactericidal effect (3600 – 8500 ml/cm^2) (Kikuchi *et al.*, 1997; Choi *et al.*, 2007) in comparison to chloramine (95 – 180 ml/cm^2) (Hoff, 1986) or ozone (0.0007 –0.02 ml/cm^2) (Hunt & Marinas, 1997).

The antibacterial properties of nAg have been proposed due to their size and shape (Morones *et al.*, 2005; Pal *et al.*, 2007). Results of the effect of nAg in the size range 1–100 nm on the growth of four Gram-negative bacteria (*Escherichia coli*, *Vibrio cholerae*, *Pseudomonas aeruginosa* and *Salmonella typhus*) suggested that growth of the bacterial cultures (5×10^7 colony forming units (cfu)/ml) was inhibited at concentrations exceeding 75 μg/ml. On the other hand, previous characterization of the interactions of the nAg with the bacteria using high angle annular dark field (HAADF) scanning transmission electron microscopy (STEM) showed that nanoparticles

attached to the surface of the cell membrane or located inside the bacteria were mainly in the size range of 1–10 nm (Morones *et al.*, 2005). For the first time, shape dependent antibacterial properties were reported by Pal et al. (Pal *et al.*, 2007) suggesting that truncated triangular silver nanoplates exhibited stronger biocidal action when compared with spherical and rod-shaped nanoparticles and with Ag^+ (in the form of $AgNO_3$).

The antibacterial activity of silver ion (Ag^+) and related silver species, and to a lesser extent nAg have been studied extensively (Morones *et al.*, 2005; Shrivastava *et al.*, 2007; Yoon *et al.*, 2007), however, the exact mode of action for the nAg on bacteria is presently partially unknown. Several propositions have been advanced to explain this phenomenon. First, the catalytic oxidation by metallic silver and reaction with dissolved monovalent silver ion was viewed as likely contributing factor to the bactericidal effect (Ju-Nam & Lead, 2008). Alternatively, this was explained based on the electronspin resonance spectroscopy studies of nAg showing the damage of the bacterial membranes may have been induced owing to the formation of free radicals (Danilczuk *et al.*, 2006; Kim *et al.*, 2007).

Other form of nanoparticles used as water disinfectant are the $nTiO_2$ through the photodegradation process due to UV light irradiation, and the complete mineralization of toxic organic pollutants. This phenomenon successfully was applied in environmental technology for wastewater and groundwater treatment, removal of benzothiophene from diesel fuel, degradation of air pollutants (e.g. nitrogen oxide, sulforoxides and volatile organic compounds), and in the killing of bacteria, fungi, algae and viruses (Shephard *et al.*, 2002). For example, using *E. coli* as the model organism, the bactericidal activity of TiO_2/UV photocatalysts properties have been demonstrated with enhanced effect due to use of TiO_2 nanorods (Joo *et al.*, 2005). Alternatively, this is achieved through doping using either iron (Fe(III)) (Egerton *et al.*, 2006) or silver (Ag) (Page *et al.*, 2007). However, despite of the large specific surface area of $nTiO_2$ the development of commercial applications is slow chiefly because of their tendency to aggregate and coalesce very easily forming larger particles. Such undesirable effect lowers the catalyst efficiency, and requires complex procedures to separate and recover the $nTiO_2$ particles from the reactant mixture (Yu *et al.*, 2002)

The forgoing few examples illustrate the nanotechnology-based solutions potential in addressing water-related challenges in the developing world including Africa. Therefore, the potential for nanoparticles to offer alternative technologies to support the provision of clean water, increase water access, and clean up the environment in the context of the developing countries is beyond debate. However, there are both technical and environmental risk aspects that are outstanding – which in the view of the authors should adequately be addressed before full scale commercialization of these technologies.

Nanotechnology: health-related applications

Nanotechnology offers numerous advantages in comparison to the traditional drug design, delivery, and medical diagnostics approaches primarily due to the possibility of controlling and manipulating structure at the molecular level. For example, in pharmaceuticals – nanotechnology has made the dissolution rates higher and faster, have increased the bioavailability of many drugs, and improved the stability of sensitive agents. This is because it has been shown that nanoparticles can be engineered to (i) recognise diseases at the cellular level, (ii) provide visual imaging of affected organs (through imaging studies), and (iii) deliver the therapeutic compounds. Currently, there are enormous scientific efforts in improving the treatment of cancer using nanotechnology-enabled therapeutic drugs, however, the high prevalence of epidemic infectious diseases particularly the human immunodeficiency virus (HIV) responsible for causing acquired immunodeficiency syndrome (AIDS) (HIV/AIDS), tuberculosis (TB), and malaria in the developing countries – merits special attention in order to reduce, manage or eliminate the present unacceptable disease burden these diseases have impacted in the society particularly in Africa as shall be presented in the latter section. HIV/AIDS and malaria will be discussed in the context of nanotechnology application to illustrate this possibility.

Diagnostics for the HIV/AIDS

Presently, the HIV/AIDS is a global challenge and though the conventional drug delivery approaches including the HAART have shown the capability to increase the life span of the patients, however, serious limitations to achieve total eradication of the HIV remains. One way

of bringing the pandemic under control is to exploit the capability of nanotechnology platforms currently at pre-clinical, and research and development phase. Comprehensive reviews on the potential of nanomedicines for the treatment of HIV/AIDS have been presented recently (das Neves *et al.*, 2010; Gunaseelan *et al.*, 2010; Gupta & Jain, 2010) with special emphasis on their application in the developing world. In this chapter, only a few salient aspects are highlighted. The application of nanotechnology in the treatment of HIV/AIDS is partly premised in addressing the limitations of the current antiretroviral therapies (Gupta & Jain, 2010), and secondly to enhance the treatment effectiveness, efficiency and reduction of costs (Wong *et al.*, 2010).

For example, it has been reported that HAART are generally less ineffective for the treatment of central nervous system (CNS) complications than other AIDS-related illnesses (Hammer *et al.*, 2008). As a result, even though HAART remains fairly effective against the CNS illnesses, however, it is ineffective to more severe cases such as HIV-associated dementia (HAD). Consequently, this leads to high numbers of HAD patients living with HIV/AIDS as their lives are prolonged. In addition, the inability of these drugs from completely abolishing or reducing the viral loads considerably in the CNS potentially allows latent infection (Blankson *et al.*, 2002) which can promote the development of drug resistance – multi-drug resistance (MDR) and as result limit the effectiveness of the antiretroviral therapy (Amiji *et al.*, 2006). Because of the inefficiencies of the present HAART regimens, it is estimated that up to 7.7 years may be required for uninterrupted treatment to eliminate the HIV viral load during the early phases of infection (Chun *et al.*, 2007). Clearly such long periods of treatment are undesirable due to potential increase in risks like liver dysfunctions, peripheral neuropathy, metabolic complications, as well as high drug costs, patients' non-compliance, and possible drug-drug interactions (Temesgen *et al.*, 2006). And finally, the current HAART are limited or fail to deliver the drugs into the brain (Wong *et al.*, 2010). Also, the current conventional methods are limited in providing sustained-release and delivery of active molecules to the target sites (das Neves *et al.*, 2010).

To address the above challenges in pursuit of improving the management and treatment of the HIV/AIDS, several nanotechnology-based treatment therapies have been proposed and are under

research and development or pre-clinical phase as mentioned earlier. To enhance the delivery of the ARVs into the CNS a number of nanocarriers have been studied in *in vitro* or in animal models (Spitzenberger *et al.*, 2007; Govender *et al.*, 2008). Three nanocarriers broadly classified as polymer/dendrimer-based, lipid-based and micelle-based have been developed. However, only a few that are suitable candidates for drug delivery into the brain have been identified. The criteria for the selection of a nanocarrier include; being non-toxic, fully biodegradable as well as producing well-characterized and harmless degradation products.

One of the innovative and feasible pathways of using nanocarrier-based delivery for the HIV/AIDS drugs is the multi-functionalization of the nanocarrier system (Gupta & Jain, 2010). Multi-functionalization of the nanocarrier allows the incorporation of several therapeutic agents (e.g. HAART) into one formulation for maximum clinical effect. Secondly, it allows the drugs to be effectively targeted to the desired site using the multifunctional nanocarriers. It appears from the extensive review of studies reported to date (see for example reviews by Gupta and Jain and Wong et al. (Gupta & Jain, 2010; Wong *et al.*, 2010), that the solid lipid nanoparticles (SLN) and liposomes are among the most suitable candidate nanocarriers for the HIV/AIDS drug therapeutic delivery. This is because they are biocompatible, safe, versatile and flexible, stable as well as technically feasible for fabrication at industrial scale at reasonable costs. That means the SLN and liposomes offer tremendous possibilities in the clinical application of nanotechnology for the treatment of HIV/AIDS infections in the coming years. Therefore, it is premised that such a drug delivery nanocarrier-based system would find great appeal in the developing world – including Africa – not only because of superior clinical efficacy, lower costs but also due to ease of administration particularly in very remote regions.

Diagnostics for malaria

Malaria is the most prevalent parasitic infectious disease to humans caused by the *plasmodium* genus. The *plasmodium* genus are broadly classified as; *Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae* and *Plasmodium ovale* – and transmitted to humans by female mosquito vector of the *Anopheles* genus. Malaria is the leading parasitic infectious disease

imposing the highest mortality and morbidity globally, and particularly in the developing countries (Urdea *et al.*, 2006; Yager *et al.*, 2006).

One of the challenges is the intractable difficulties in the disease control because of the parasite complex lifecycle (Gardella *et al.*, 2008; Greenwood *et al.*, 2008) and the increasing number of immune-compromised patients that suffer from malaria and HIV/AIDS co-infections (Skinner-Adams *et al.*, 2008). Another factor is the complexity of the recommended regimens – which are usually a combination of two or more drugs. The latter factor contributes to rapid increase in the drug costs and a reduction in patient compliance mainly associated with severe side effects (Santos-Magalhaes & Mosqueira, 2010). Furthermore, extrinsic factors like technical and operational failures in implementing campaigns to fight malaria, poor quality of medicines distributed in different countries, drug-drug interactions, the unavailability of less toxic drugs, resistance of the vector to insecticides and socioeconomic conditions of affected populations aggravate the difficulties for the eradication of malaria in the world (Winstanley & Ward, 2006). Up to now, a suite of tools and methods have been developed to reduce or eliminate the widespread dissemination of malaria through measures such as the prevention of infection, preventive treatment using antimalarial drugs, and treatment with artemisinin-based combination therapy (ACT) (Santos-Magalhaes & Mosqueira, 2010).

It is in the context of the above setting compounded by the small number of new drugs or innovative antimalarial medicines approved since 1990, the search for more efficient and less toxic antimalarials, the development of a successful vaccine, and the design of nanotechnology-based delivery systems applied to drugs and antigens are likely to be the main strategies in combating this disease in future. The research efforts towards the development of nanocarriers are currently at the research and development stage where several nanosized delivery systems have shown positive effectiveness in animal models and prophylaxis of malaria. Nanocarriers are useful tools to improve the pharmacokinetic profile of effective drugs characterized by poor water solubility, low bioavailability and high intolerable toxicity which posed serious limitations to the pharmacotherapy (Forrest & Kwon, 2008).

A number of nanocarriers namely; colloidal liposomes, polymeric nanoparticles, lipid nanoparticles including lipid drug conjugate (LDC) nanoparticles, solid lipid nanoparticles (SLN), and polymer chitosan have been proposed for the optimization of anti-malarial drugs delivery to treat malaria infections. An example of promising anti-malarial agents is the phosphorothioate antisense oligodeoxynucleotides (ODNs) in silencing malarial topoisomerase II gene especially to address the increasing drug resistance of *P. falciparum* (Foger et al. 2006). However, the drug's effectiveness is hampered by poor stability and limited intracellular penetration. To overcome these limitations, Foger et al (Foger *et al.*, 2006) showed that ODNs complexed with the biodegradable polymer chitosan to form solid nanoparticles increases the susceptibility of *P. falciparum*. In that study, nanoparticles were found to protect ODNs from nuclease degradation. *P. falciparum* K1 strain was exposed to the chitosan/ODN-nanoparticles for 48 h in order to examine the effects of chitosan/antisense (AS) and chitosan/sense (S) oligodeoxynucleotide nanoparticles on malaria parasite growth.

Both negatively and positively charged antisense nanoparticles as well as free antisense ODNs (in a final concentration of 0.5 μM) showed sequence specific inhibition compared with sense sequence controls. Notably, nanoparticles were much more sequence specific in their antisense effect than free ODNs. For instance, nanoparticles with negative surface charge exhibited a significantly stronger inhibitory effect (~87% inhibition) on the parasite growth in comparison to the positive ones (~74% inhibition) or free ODNs (~68% inhibition) (Foger *et al.*, 2006). Furthermore, the use of nanoparticles demonstrated more pronounced sequence specific antisense effects as compared to free ODNs likely due to sustained release of ODNs from chitosan nanoparticles hence lowering the initial concentration – results which are in agreement with earlier findings (Barker *et al.*, 1998; Noonpakdee *et al.*, 2003). This confirms ODNs inhibit cellular gene expression in a specific sequential manner at low concentrations.

Another example is the encapsulation of the quinine (CQ) in long-circulating liposomes. The drug release kinetics was evaluated mimicking physiological fluids and endosome environments (Wong *et al.*, 2006). CQ was highly encapsulated in neutral conventional and PEGylated liposomes using a transmembrane pH gradient method to improve the encapsulation efficiency. Initially, blank conventional liposomes were prepared with SPC and CHOL, or PEGylated

liposomes using 5 mol% PEG 2000 grafted onto DSPE-PEG2000 and CHOL. Thereafter the entrapment of the drug was performed in neutral liposomes by an imposed pH gradient. Finally, the CQ-loaded liposomes were lyophilized using trehalose as cryoprotectant. The highest CQ efficiency of encapsulation was 99% before lyophilization and 87% after hydration of the lyophilized form for an internal pH of 3.6 (0.2M). The *in vitro* release profile of CQ was different, considering the pH of the internal phase of liposomes and the pH of the release medium (7.4 and 5.5). For conventional liposomes, the cumulative release of CQ at physiological pH 7.4 was 30% within 6 h, while more than 90% of the drug was released from liposomes at pH 5.5. In contrast, PEGylated liposomes significantly reduced the release of CQ from liposomes at pH 5.5 (Wong *et al.*, 2006).

The above two examples have shown the possibilities provided by the pharmaceutical nanotechnology in improving the efficacy of the antimalaria drugs to overcome the challenges of the conventional delivery systems such as poor solubility, chemical instability, inadequate bioavailability profiles and intolerable toxicity. This is due to the possibility of manipulating physicochemical properties of nanocarriers (e.g. surface reactivity, surface charge, etc) aimed at improving antimalarial drugs selectivity; however, these drugs development are at research and development phase, and only after some years before their full potential to treat infectious malaria disease will be realized. Recent detailed review of the current nanotechnology-based antimalaria drugs advances have been presented by Santos-Magalhães and Mosqueira (Santos-Magalhaes & Mosqueira, 2010).

Health Effects of nanomaterials

Concerns have been raised that the very desirable properties of nanoparticles exploited for their beneficial applications might also be the reason for their toxicity. With the knowledge that many applications of nanotechnologies may pose new risks, international agencies have established working groups to consider their potential risks to health and environment during manufacture, use and disposal in order to ensure their beneficial applications without sacrificing their safety.

The hazardous properties and their health effects of newly synthesized nanoparticles and nanomaterials have been investigated using *in vitro* and *in vivo* animal systems. Using experimental animals, the behavior of nanoparticles and nanomaterials and their distribution to target organs following exposure via inhalation, ingestion or through the skin, were studied. Using cells that represented these target organs their toxicity and their partition within different cellular compartments were investigated. These studies were essential for proper risk assessment which requires understanding of the toxicological hazards associated with these materials and of the levels of exposure, which may produce these toxicities.

It is important to emphasize at this stage that many of the nanoproducts may pose no risk to health or to the environment if they are fixed to or are incorporated within a material. It is the exposure to free manufactured nanoparticles and nanotubes in the production stage or during their release from the fixed or embedded composites that will be of major concern. A short summary of the identified adverse effects of free nanoparticles and nanotubes will therefore be presented in this section that have been discussed earlier which are also those that are presently being synthesized in South Africa to create awareness on their toxicity and urge the researchers as well as industry to take the necessary precautions to make their products safer in their applications.

Gold nanoparticles

Size and functional groups on the surfaces of gold nanoparticles were found to determine their toxicity. Initial reports suggested that gold nanoparticles with functional cationic side chains are likely to be toxic to mammalian and bacterial cells (Goodman *et al.*, 2004) whereas the toxicity of anionic surface modifier was found to be dependent on the property of functional group present. On the other hand, gold nanoparticles with citrate and biotin surface modifier did not reveal obvious toxic, nonetheless, glucose and cysteine were found to be (Connor *et al.*, 2005). On other hand, layer-by-layer polyelectrolyte (PE) coated gold nanorods were found to be of low toxicity and therefore recommended for applications such as thermal cancer therapy (Hauck *et al.*, 2008).

In addition, to the functional groups, the size of the gold nanoparticles did also influence their toxicity. For example, it was found that in spite of efficient uptake into human cells by endocytosis, AuNPs with 18 nm show little cytotoxicity (Shukla *et al.*, 2005) . Consistent with this observations, others have found that particles of 1–2 nm in size were highly toxic and AuNPs larger than 15 nm were not toxic (Pan *et al.*, 2007). Cytotoxicity also depended on the type of cells used. For example, 33 nm citrate-capped gold nanospheres were found to be noncytotoxic to baby hamster kidney and human hepatocellular liver carcinoma cells, but cytotoxic to a human carcinoma lung cell line at certain concentrations (Patra *et al.*, 2007). Moreover, 10-, 20-, and 40-nm gold particles conjugated with anti-protein A antibodies for targeting the bacterial surface were shown to be selectively toxic to Gram-positive bacterium *Staphylococcus aureus* (Zharov *et al.*, 2006). Recent excellent review has summarized data on cytotoxicity of many types of nanomaterials including gold nanoparticles (Lewinski *et al.*, 2008).

Several groups have also examined translocation and tissue distribution of gold nanoparticles. Rats exposed to gold particles with diameters of 5-8 nm have shown that a large portion of the deposited gold particles was retained in the lung tissue and also alveolar macrophages. In addition, a low but significant increase of gold was found in the blood indicating systemic particle translocation (Takenaka *et al.*, 2006). A similar systemic translocation was also found following ingestion of colloidal gold particles in mice. In addition, absorption in the animals' brain, lungs, heart, kidneys, intestines, stomach, liver and spleen, were more pronounced for 4 and 10 nm nanoparticles, in comparison with 28 and 58 nm particles (Hillyer & Albrecht, 2001). On the other hand, Paciotti et al. (2004) (Paciotti *et al.*, 2004) studied colloidal gold nanoparticles injected intravenously in mice in which they had implanted colon tumour cells. Nanoparticle distribution occurred preferentially at the tumour site, without significant accumulation in the liver, the spleen or the animals' other organs. Similarly, Hainfeld et al. (Hainfeld *et al.*, 2004) have shown that gold nanoparticles in solution, injected intravenously into mice with induced breast tumours, were found in the kidneys 5 minutes after injection and then were located preferentially at the tumour site and, to a lesser degree, in the liver. It was concluded that this type of formulation may be of low toxicity. On the other hand, the acute toxicity of 13 nm PEG-coated gold nanoparticles was recently confirmed (Cho *et al.*, 2009). The intracellular distribution of gold nanoparticles were also found to be size dependent for their

localization into vesicles (Chithrani *et al.*, 2006) with (Pernodet *et al.*, 2006) or without (Gu *et al.*, 2009) nuclear penetration.

Silver nanoparticles

In vitro skin penetration of silver nanoparticles, coated with polyvinylpirrolidone, with intact and damaged human skin was studied and was found that silver nanoparticle absorption through intact and damaged skin was very low but detectable (Larese *et al.*, 2009). Silver nanoparticles were also found to be cytotoxic to cultured human fibroblasts and keratinocytes (Chen & Schluesener, 2008) and to rat liver derived cell line (BRL 3A) (Hussain *et al.*, 2005) *in vitro.* At the same time, silver nanoparticles were also found to interact size-dependently with HIV-1 via preferential binding to the gp120 glycoprotein knobs and thus inhibiting the virus from binding to host cells, as demonstrated *in vitro* (Elechiguerra *et al.*, 2005).

The *in vivo* toxicity and pathogenicity of silver nanoparticles was also investigated. A 28-day inhalation exposure study in Sprague-Dawley rats found that both male and female rats did not show any significant changes in the hematology and blood biochemical values in either male or female rats with no significant changes in body weight relative to all the concentrations of silver nanoparticles during entire experimental period except hyperplasia in bile-duct (Ji *et al.*, 2007). A 28-day oral exposure, again in Sprague-Dawley rats, could not find any hyperplasia in bile-duct, indicating that a higher dose with prolonged exposure is needed to induce these responses (Sung *et al.*, 2008). A subchronic 90-day inhalation study could however find that lungs and liver were the major target tissues for prolonged silver nanoparticle accumulation. Bile-duct hyperplasia could also be noted in both the male and female animals with a higher accumulation of silver nanoparticles in the female kidneys (Sung *et al.*, 2009).

Nanoscale Zero-Valent Iron (nZVI)

As nZVI may form iron oxides, it is therefore generally considered to be of minimal toxicity. Little is known about the toxicity specific to nZVI but ZVI is known to produce Fe^{2+} and iron oxides through oxidation and therefore, nZVI may catalyze the formation of hydroxyl radicals

($OH\cdot$) from superoxide (O^{2-}) and hydrogen peroxide (H_2O_2) free radicals through this transformation process (Li *et al.*, 2009a). Subsequently, number of studies has been conducted to assess the toxicity of nZVI. For example, Phenrat et al. (Phenrat *et al.*, 2009) have shown that nZVI could induce oxidative stress on mice BV2 microglia cells. Similar observations were also made on medaka fish (*Oryzias latipes*) and their embryos in the ability of nZVI to produce oxidative stress (Li *et al.*, 2009b). Microorganisms in groundwater and soil in the remediation area are also able to accumulate nZVI particles and therefore affect the toxicity (Lee *et al.*, 2008).

Titanium dioxide nanoparticles

Short-term inhalation studies of male Wistar rats were exposed to different concentrations of TiO_2 nanoparticles for 6 h/day for 5 days resulted in morphological changes in the lung, with the highest tested concentrations of 50 mg/m^3 producing an increase in lung weight and in inflammation associated with dose-dependent increases in bronchoalveolar lavage fluid (BALF) total cell and neutrophil counts, total protein content, enzyme activities and levels of a number of cell mediators (Ma-Hock *et al.*, 2009a). Translocation and distribution of TiO_2, subsequent to pulmonary exposure has also been investigated, with a particular focus on the transfer of particles to the brain. *In vivo* studies have indicated that following nasal instillation, both forms of TiO_2 nanoparticles, rutile and anatase have translocated to the brain, with their accumulation within the cerebral cortex, thalamus and hippocampus. It was postulated that this transport may have occurred via the olfactory bulb neuronal transport as it was unlikely to be mediated via penetration into the cardiovascular system and via the blood (Wang *et al.*, 2008a). It was later confirmed that hippocampus was the main target of accumulation and toxicity of TiO_2 (Wang *et al.*, 2008b). On the other hand, systemically available TiO_2 nanoparticles, as simulated by the i.v. injection, was trapped mainly in the liver and spleen (van Ravenzwaay *et al.*, 2009).

Parameters that affected the toxicity of TiO_2 were also investigated. For example, size and the crystalline nature of the TiO_2 nanoparticles were found to determine their toxicity *in vivo*. For example, results have shown that inert particles can become biologically active when nano-

scaled (Zhang *et al.*, 2005) and that nanoscale titanium dioxide could increase pulmonary inflammation parameters 10 times more than administration of fine particles of the same products (Donaldson *et al.*, 2001). With *in vivo* inhalation studies with rats, TiO_2 nanoparticles could also be shown that the nanoscale TiO_2 could be retained by the lung and their clearance was found to be much slower than their larger counterparts (Ferin *et al.*, 1992; Oberdorster *et al.*, 1994; Renwick *et al.*, 2004). Similar inhalation studies with mice, the highly crystalline anatase of TiO_2 was found to be more toxic than a mixture of rutile and anatase (Grassian *et al.*, 2007) . The pathological response following pulmonary exposure to TiO_2 within the lung were found to be emphysema-like in nature with more pronounced lesions in areas where particles preferentially accumulated, with an inflammatory response (Chen *et al.*, 2006). Inhalation studies using rat, mice and hamster found that rat was the most sensitive and hamster the least sensitive species to the effects of TiO_2 indicating that the choice of species may influence the pulmonary response to TiO_2 nanoparticles (Bermudez *et al.*, 2004). Maternal exposure to anatase TiO_2 nanoparticles was also investigated. It was found that such an exposure have caused in the offspring the changes in the expression of genes associated with brain development, cell death, response to oxidative stress, and mitochondria in the brain during the perinatal period, and those associated with inflammation and neurotransmitters in the later stage (Shimizu *et al.*, 2009)**.**

In vitro investigations using a variety of lung cell models were conducted to assess TiO_2 toxicity. Using the human lung bronchial epithelial cells BEAS-2B, a dose and time dependent decrease in cell viability was observed by 21 nm TiO_2 nanoparticles with a concomitant increase in reactive oxygen species production and depletion in glutathione, implying that an oxidative mechanism was involved in this cytotoxic response (Gurr *et al.*, 2005). Using alveolar epithelial type 2 cell line A549, crystal structure-dependent cytotoxicity of TiO_2 was observed where it was found that the greater the anatase content of the sample, the greater the ability of the TiO_2 nanoparticles to induce cell death (Simon-Deckers *et al.*, 2008). Using rat tracheal explants, it could be shown that 21 nm TiO_2 nanoparticles could stimulate growth factor expression (such as platelet-derived growth factor (PDGF)) and could enhance pro-collagen expression (Churg *et al.*, 1999). Finally using rat alveolar macrophages obtained from bronchoalveolar lavage, a dose-dependent decrease in cell viability could be observed (Kim *et*

al., 1999). These *in vitro* investigations have therefore confirmed the observation with the *in vivo* experiments that size and the crystalline nature of TiO_2 nanoparticles will determine their toxicity and that oxidative stress is the main mechanism for this toxicity. Finally, *In vitro* studies have also shown that coating of TiO_2 may influence their toxicity. For example, it was shown that uncoated nanosized anatase TiO_2 and fine rutile TiO_2 are more efficient than SiO_2-coated nanosized rutile TiO_2 in inducing DNA damage in human bronchial epithelial BEAS 2B cells, whereas only nanosized anatase is able to slightly induce micronuclei (Falck *et al.*, 2009).

The use of TiO_2 in sunscreens and cosmetics has prompted number of investigations to assess the dermal penetration and toxicity of TiO_2 nanoparticles. *In vivo*, and in *vitro,* have shown that the majority of the TiO_2 was contained within the stratum corneum, with minimal distribution within the epidermis (Schulz *et al.*, 2002). Using HaCaT keratinocytes, human dermal fibroblast cells, SZ95 sebaceous gland cells and primary human melanocytes, it could be seen that the TiO_2 nanoparticles were internalized and were evident in the cytoplasm and perinuclear region of fibroblasts and melanocyte and that this internalization was associated with an increase in intracellular calcium. No particle uptake or alterations in calcium signalling were observed within keratinocytes or sebocytes. On the other hand, a dose and time dependent decrease in cell proliferation was evident within all cell types, and an increase in cell death (via apoptosis) within fibroblasts was apparent (Kiss *et al.*, 2008). Similarly, using mouse L929 fibroblasts, it was also possible to show time and dose dependent decrease in cell viability induced by TiO_2 nanoparticles. In addition, it was possible to show the internalization of these nanoparticles by phagocytosis, and their containement within lysosomes with an increase in ROS production and decreases in GSH and SOD activities (Jin *et al.*, 2008).

Finally, a number of ecotoxicological studies were carried out using short-term toxicity of TiO_2 NPs to algae, daphnids, juvenile and adult zebrafish and were found to be of low toxicity (Griffitt *et al.*, 2008). However, independent of direct toxic effects, the presence of TiO_2 nanoparticles was found to cause indirect effects, for example by influencing toxicity and bioaccumulation of other pollutants present in the aquatic environment. Indirect effects can also be a result of environmental pollutants adsorbing onto the particles. For example, the enhanced accumulation of cadmium (Cd) and arsenic (As) found in carp (*Cyprinus carpio*) in the presence of TiO_2 NPs

(Zhang *et al.*, 2007) was attributed to facilitated transport into different organs. On the other hand, sub-acute toxicity studies of TiO_2 NPs on this same aquatic organism, have shown depletion in antioxidant enzyme activities and the elevation of LPO with a concomitant necrosis and apoptosis hepatocytes with gill pathologies including edema and thickening of gill lamellae as well as gill filaments, indicating a potential risk from TiO_2-NPs released into the aqueous environment (Hao *et al.*, 2009). As only a few studies describe TiO_2 NP toxicity to algae (Aruoja *et al.*, 2009) , the potential carrier effect of TiO_2 for other pollutants through a series of experiments, designed to reveal the influence of TiO_2 particles on the algal toxicity of cadmium was most recently investigated. It was found that in addition to particle toxicity, potential interactions with existing environmental contaminants are also of crucial importance in assessing the potential environmental risks of nanoparticles (Hartmann *et al.*, 2009).

Zinc oxide nanoparticles

Given the intensive application of nanoscale zinc oxide (nZnO), growing concerns have been expressed about its health and environmental impacts. The effect of ZnO nanoparticles on numerous prokaryotic and eukaryotic as well as on plant cell systems was therefore investigated. For example, Gojova *et al* have shown that *in vitro* incubation of human aortic endothelial (Gojova *et al.*, 2007) and mouse neuroblastoma cells (Jeng & Swanson, 2006) with nZnO have caused 50% reduction in their viability; Incubation of mesothelioma MSTO-211H or rodent 3T3 fibroblast with these nanoparticles have caused their complete death (Brunner *et al.*, 2006). On the other hand, they were only slightly toxic to human T cells (Reddy *et al.*, 2007) but very toxic to human pulmonary cell lines: A549 and THP-1 cells (Lanone *et al.*, 2009). *In vivo* exposure to nZnO have produced potent but reversible inflammation which was resolved by 1 month postinstillation exposure (Sayes *et al.*, 2007).

The toxicity of nZnO against number of pathogenic bacteria was also investigated. Once again, a comparative toxicity study between different metal oxides has shown that ZnO was the most toxic nanoparticles against *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas fluorescens, Escherichia coli* (Adams *et al.*, 2006) and *Streptococcus agalactiae* and *Staphylococcus aureus* (Huang *et al.*, 2008) and thus confirming the bactericidal action of nZnO on both gram-negative

and gram-positive bacteria. Their use as aerosols to control airborne disease (e.g., influenza, tuberculosis, and pneumonia) and prevent bacterial fouling was therefore suggested (Wu *et al.*, 2010).

Comparative ecotoxicity studies on metal oxide nanoparticles have indicated that ZnO nanoparticles were always most toxic to *Pseudokirchneriella subcapitata* algal growth (Franklin *et al.*, 2007; Aruoja *et al.*, 2009) and to zebrafish embryos and larvae (Zhu *et al.*, 2008) and that this toxicity could be attributed to the solubilized Zn^{2+} (Franklin *et al.*, 2007; Aruoja *et al.*, 2009). A similar comparative phytotoxicity study on metal oxide nanoparticles have also confirmed that nZnO were most toxic on the development of *Arabidopsis thaliana* (Mouse-ear cress) assessed by their effect on seed germination, root elongation, and number of leaves. In this instance, however, zinc dissolution could not solely account for the observed toxicity as direct exposure to nanoparticles significantly could contribute to this phytotoxicity (Lee *et al.*, 2010). A similar effect of ZnO nanoparticles on seed germination and root growth of six higher plant species (radish, rape, ryegrass, lettuce, corn, and cucumber) was also reported (Lin & Xing, 2007).

Several of these studies have indicated that the solubilized Zn^{2+} is the cause of these toxic effects. For example, this was suggested to be the cause of toxicity of nZnO to crustaceans *Daphnia magna* and *Thamnocephalus platyurus* and protozoan *Tetrahymena thermophila* (Blinova *et al.*, 2010). Other studies have shown that metal NPs may be more toxic than either their ionic forms or their parent compounds (Navarro *et al.*, 2008; Farre *et al.*, 2009). For example, it was shown that nZnO killed zebrafish embryos (50 and 100 mg/L), retarded the embryo hatching (1–25 mg/L), reduced the body length of larvae, and caused tail malformation after the 96 hpf exposure. $Zn_{(dis)}$ only partially contributed to the toxicity of nZnO (Bai *et al.*, 2009). The same was true for nematode *Caenorhabditis elegans* where the oxide solubility influenced the toxicity of ZnO, but nanoparticle-dependent toxicity was also observed (Wang *et al.*, 2009).

Similar contradictory observations were also made for the toxicity of nZnO to mammalian cells. For example, in mouse neuronal stem cells, it was concluded that the nZnO toxicity comes from

the dissolved Zn^{2+} in the culture medium or inside cells (Deng *et al.*, 2009) confirming earlier studies that the dissolved Zn^{2+} from zinc-containing compounds would more easily affect the function of neuro cells, causing neurotoxicity (Takeda *et al.*, 1997; Persson *et al.*, 2003). The same was proposed for the toxicity of ZnO to RAW 264.7 and BEAS-2B cell lines (Xia *et al.*, 2008).

Biodegradable polymeric nanoparticles

When using nanoparticles as vehicle for drug delivery, the health effects of the residual material after drug delivery should be considered. It is therefore desirable to use nanoparticles that are biodegradable. Poly(ester) nanoparticles are said to be nontoxic and biodegradable (Tracy *et al.*, 1999) . On the other hand, surface modified PLGA such as chitosin-PLGA nanoparticles were found to be toxic to certain cell types (Nafee *et al.*, 2009). The cytotoxicity of both PAMAM and poly(propylene imine) (PPI) dendrimers is very much dependent on size and also on the nature and density of the surface charged groups where in general, cationic charges are found to be more toxic (Mishra *et al.*, 2009). For example, a concentration dependent tendency to cause haemolysis and changes in erythrocyte morphology has been linked to the presence of $–NH_2$ groups. In contrast to PAMAM dendrimers PPI dendrimers with DAB and DAE cores did not show generation dependence for the haemolytic effect (Malik *et al.*, 2000). On the other hand, dendrimers with carboxylic acid terminal functional groups, are not toxic to zebrafish embryos (Heiden *et al.*, 2007). It is therefore recommended to modify the surface amine groups of PAMAM and PPI dendrimers with neutral or anionic moieties to avoid the toxicity and liver accumulation associated with their polycationic surfaces (Malik *et al.*, 2000; Jevprasesphant *et al.*, 2003). Subsequently, when PEGylated dendrimer was evaluated for acute toxicity in vivo, no toxicity, mortality or abnormal blood chemistry was observed in doses up to 2.56 g/kg ip and 1.28 g/kg iv (Chen *et al.*, 2004).

Carbon nanotubes

Potential health effects of carbon nanotubes were of concern due to their similarity to asbestos fibres (Pacurari *et al.*, 2010). Great number of *in vitro* and *in vivo* studies has therefore been

conducted to assess their toxicity and pathogenicity. For example, *in vivo* experiments with SWCNT have shown their ability to translocate (Wang *et al.*, 2004) and distribute to different organs as well as accumulate in the cell nucleus (Pantarotto *et al.*, 2004). Intravenous injection of acid-oxidized MWCNTs and Tween-80-dispersed MWCNTs have produced severe liver damage with the latter producing more severe effects (Ji *et al.*, 2009). Ocular instillation could produce no adverse effects (Huczko & Lange, 2001) but exposure through the skin could result in dermal penetration and toxicity due to generation of free radicals, oxidative stress, and inflammation (Murray *et al.*, 2009).

Inhalation studies have found that MWCNTs could produce pathological changes in the lung (Ma-Hock *et al.*, 2009b) as well as alteration in systemic immune function (Mitchell *et al.*, 2007). Intraperitoneal instillation to MWNNT of mice could result in asbestos-like, length-dependent, pathogenic behavior including inflammation and formation of granulomas (Poland *et al.*, 2008) and mesotheliomas in p53 heterozygous mice (Takagi *et al.*, 2008) and in Fischer 344 rats (Sakamoto *et al.*, 2009). Furthermore, an investigation of molecular signalling on normal mesothelial and malignant mesothelial cells *in vitro* has revealed that SWCNTs were able to produce similar molecular events as asbestos. Using the same cell types, these authors could also show that MWCNT containing low iron content generated only negligible amounts of reactive oxygen species but has caused a parallel activation of two important transcription factors. It was therefore concluded as in SWCNT that MWCNT are biologically potent activators of molecular events in normal cells associated with mesothelioma development (Pacurari *et al.*, 2008a; Pacurari *et al.*, 2008b).

Their incubation with human lung fibroblasts, could cause direct fibrogenic effects (Wang *et al.*, 2010) and with human bronchial epithelial BEAS 2B cells could produce genotoxic effects (Lindberg *et al.*, 2009). These cytotoxic responses of cells in culture were found to be dependent on the presence of functional groups where an increase of sidewall functionalization decreased SWNT toxicity to human dermal fibroblasts (Sayes *et al.*, 2006). Multi-walled carbon nanotubes could also produce similar effects as to those observed with SWCNT. The incubation of these nanotubes with human epidermal keratinocytes *in vitro* could decrease cell viability and a significant increase in an inflammation marker (interleukin-8) (Monteiro-Riviere *et al.*, 2005). A

comparative study between the cytotoxicty of single walled and multi-walled carbon nanotubes on alveolar macrophages in Guinea pigs (Jia *et al.*, 2005) genotoxicity on murine macrophage cell line RAW 264.7 (Kagan *et al.*, 2006) have shown that SWCNT have higher toxicity than MWCNT.

If released in the environment, nanomaterials might be inhaled by populations and cause damage to the deepest regions of the respiratory tract, i.e., the alveolar compartment. To model this situation, Simon-Deckers et al (Simon-Deckers *et al.*, 2008) have studied the response of A549 human pneumocytes after exposure to aluminium oxide or titanium oxide nanoparticles, and to multi-walled carbon nanotubes where size, crystalline structure and chemical composition was investigated. It was found that carbon nanotubes were more toxic than metal oxide nanoparticles.

Conclusions

In this chapter, through the use of basic building blocks of nanostructures entailing the development of nanoscale materials hinged on advances in chemistry have demonstrated their potential in addressing part of the MDGs – with particular emphasis on the African continent. This is through the application of nanotechnology-based products and services aimed at improving; the provision of clean water, the quality of the environment, and the treatment of pandemic diseases particularly HIV/AIDS and malaria – which are among the chief causes of mortality and morbidity in Africa annually. This is because the materials fabricated based on nanotechnologies are expected to be of low cost, high efficiency, and able to provide effective applications particularly for treating diseases and cleaning of drinking water in very remote regions. Such aspects are contrary to the current technologies both in water and treatment of diseases.

On the other hand, while the benefits of nanotechnology-based applications in drug therapeutics and water treatment are beyond debate, available scientific literature suggests that evidence exists for some manufactured nanoparticles and nanotubes being more toxic per unit mass than particles of the same macro-chemicals. This implies that nanoparticles potentially present a

greater risk to both humans and the ecosystems. The fundamental mechanisms of toxicity of nanoparticles may not be very different: the capacity to induce inflammation through the release of free radicals in response to a dose that is adequate to overcome the body's natural defenses. However, the difference is expected largely due to two size-dependent factors, namely, the relatively large surface area of nanoparticles, given equal mass, and their probable ability to penetrate cells more easily and in a different way. To pose a risk, these nanoparticles must come into contact with humans or the environment in a form and quantity that can cause harm. Currently, the main risk of human exposure to manufactured nanoparticles and nanotubes is in a few workplaces (including academic research laboratories) and through the use of a small number of skin preparations that contain free nanoparticles. However the current lack of available research means that the scale of this risk cannot be fully determined.

An additional concern is that increasing the use of engineered nanoparticles in industrial e.g treatment of water and nanomedicines will, very likely, lead to the release of such materials into different environmental compartments (i.e. soil, air, water and sediments). Assessment of the potential risks of such nanoparticles in the environment requires an understanding of their mobility, reactivity, ecotoxicity and persistency, however, currently is very limited or non-existent. From our review, several nanoparticles have shown their capability to cause adverse effects to organisms at different trophic levels. In spite of these challenges, it is in the view of the authors Africa stands tremendously if it gets actively involved in engaging applications enhanced by nanotechnology-driven capabilities. Therefore, it is recommended that the focus by the African authorities and researchers in the continent should not only be limited to the societal benefits of nanotechnology but also on the potential downside aspects such as toxic effects to humans and other ecosystems. Benefits of this approach include the optimal exploitation of nanotechnology unique capabilities that promotes safe, responsible and sustainable development in the target communities.

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