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Impacts of Titanium Dioxide Nanomaterials on Health, Safety and Environment

Bolaji Sadiku[1*], Adenike A. O. Ogunshe[2], Olugbenga Falode[3], Temitope Soneye[4]
[1,4]*Joint School of Nanoscience and Nanoengineering, North Carolina A & T State University, Greensboro, NC, USA*
[2]*Pegasus-Zion Community & Environmental Health, Nigeria*
[3]*Department of Petroleum Engineering, University of Ibadan, Nigeria*

***Abstract*: Nanomaterials have continued to gain increased uses across many sectors, including agricultural, industrial, and health sectors, due to their unique reactivity, mechanical and electrical properties, which are attributed to quantum effects, larger surface area, and self-assembly. Despite these, increased toxicity and attendant environmental consequences have been observed in some nanomaterials. Titanium dioxide (TiO_2) nanomaterial is known for its photocatalytic abilities, ultraviolet absorption strength, and transparency which have been useful in manufacturing some consumer products, sunscreens, light-emitting diodes, solar cells, enhanced oil recovery, cancer treatment, decomposition of organic compounds in wastewater treatment, additive in paint, cements, windows, tiles, and other products. However, detailed studies on the health impact of TiO2 nanomaterials are scanty in literature. This paper is a state-of-the-art review of the impacts TiO_2 nanomaterials in wastewater and soil have on microorganisms, plants, and humans, in relation to health, safety and environment.**

***Keywords*: Titanium dioxide, nanomaterials, toxicity, health, environment.**

1. Introduction

Nanomaterials are materials produced by nanotechnology and having particles or constituents of nanoscale dimensions. These nano-sized particles can be created from a variety of products, such as, carbon, silver, titanium, oxides, etc. Though many nanomaterials are engineered to have unique optical, magnetic, electrical, and other properties, they also exist naturally in air, smoke, and sea-spray, with incidental nanoparticles (NPs) also being created during processes such as, combustion, food milling, churning, freezing and homogenization[1]. Nanomaterials have made great impact on several industries, such as, electronics, semi-conductors, biomedical, agriculture, etc., and continue to hold great potentials in further advancing these industries. Some of these nanomaterials are so commonly useful that they are tagged, “legacy nanomaterials”, and one of these legacy nanomaterials is TiO_2 nanomaterials.

Titanium dioxide (titania) is a naturally occurring oxide of titanium[2] with a chemical formula TiO_2. The micron size TiO_2 is classified as being biologically inert in humans because it does not initiate a response or interact when introduced into biological tissues[3]. TiO_2 exists in three main forms; brookite, rutile, and anatase[4] (the most commercially used type[2]), and it used in food coloring, paints, and sunscreen. TiO_2 NPs are generally referred to as ultrafine TiO_2, and they exhibit unique properties, such as, photocatalytic abilities, ultraviolet absorption strength and transparency[5]. These unique properties have made them a choice material in consumer products, sunscreens, light-emitting diodes and solar cells, cancer treatment, decomposition of organic compounds in wastewater treatment, and as an additive to paints, cements, tiles, and other products[6]. Furthermore, several techniques exist for the synthesis of TiO_2 nanomaterials, which include deposition, oxidation[7-9], sonochemical and microwave-assisted[7, 10, 11], hydro/solvothermal, sol-gel[12] template-assisted[13], electrochemical anodization methods[14-16], thermal plasma synthesis[17] and spray pyrolysis[18].

2. Properties and Applications of Titanium Dioxide Nanomaterials

TiO_2 at the microscale is biologically inert and non-toxic and when exposed to UV light, it exhibits photocatalytic properties[7]. The valence band and conduction band are separated by a large band gap of the 3.0–3.2 eV over different phases[19]. Electrons in the valence band need to transfer to the conduction band for TiO_2 to exhibit its photocatalytic abilities and for this transfer to occur, the energy of the photon absorbed by semiconductor must be greater than the energy level of hole between two bands which is what happens when TiO_2 is irradiated with UV light[20]. The electrons in the valence band thus move to the conduction band and generate conduction band electrons and holes in the valence band.

TiO_2 nanomaterials are considered as one of the most promising semiconductors photocatalysts for energy generation and pollutant removal because of their good photocatalytic activity, low cost, assumed nontoxicity, and high stability since the discovery of hydrogen evolution through the photo-electrochemical water splitting on TiO_2 electrode[19]. The photocatalytic ability of TiO_2 nanomaterials has also been applied in the medical field for the photo-killing of bacteria on an orthopedic implant in an in vitro study. TiO_2 nanoparticle coated implants significantly inhibited the viability of bacteria when exposed to ultraviolet radiation and was able to affect the

*Corresponding author: blsadiku@aggies.ncat.edu

bacteria more than the host tissue. They are thus highly applicable in the medical field[20, 21]. TiO_2 has also been used as a photosensitizer for photodynamic therapy for endobronchial and esophageal cancers[22] and environmental applications[23].

TiO_2 nanomaterials also exhibit photocatalytic properties under visible light[20] thus broadening their possible applications. Titanium dioxide nanomaterials are used in many sunscreens because of their ability to effectively block out ultraviolet light[1, 5]. In contrast to chemical sunscreens which transform the energy of the photons into molecular conformational changes, TiO_2 nanomaterials act by scattering sunlight from the skin surface[5]. Micron-sized TiO_2 materials are known to be white in color and had poorer cosmetical appearance when compared to the chemical types but ultrafine TiO_2 is colorless, has better cosmetic appearance than chemical sunscreens and increased photo-protective effect[5].

TiO_2 NPs are of high interest to researchers due to their unique properties such as electrical conductivity, photo activity, antibacterial property self-cleaning and non-toxicity. TiO_2 is an important industrial material as it is an important component in paint, pigment, cosmetics, etc. [24]. It has also been used for optical coatings, beam splitters and anti-reflection coatings because of its high dielectric constant and refractive index. TiO_2 is believed to be most promising currently known materials due to its excellent optical properties of a high refractive index leading to a high hiding power and whiteness [25]. TiO_2 have temperature and environmentally stable dielectric properties characterized by high relative dielectric constant and low dielectric loss and have thus recently attracted attention due to their impact in fabrication of novel microelectronic devices and microwave communication systems.

Nanosized titanium dioxide, particularly in the anatase form, exhibits photocatalytic activity under ultraviolet (UV) irradiation. This photoactivity is reportedly most pronounced at the planes of anatase,[26, 27] although the planes are thermodynamically more stable and thus more prominent in most synthesized and natural anatase,[28] as evident by the often-observed tetragonal di-pyramidal growth habit. Interfaces between rutile and anatase are further considered to improve photocatalytic activity by facilitating charge carrier separation and as a result, biphasic titanium dioxide is often considered to possess enhanced functionality as a photocatalyst.[29]

The main photocatalytic characteristic of TiO_2 is a wide band gap of 3.2 eV, which can trigger the generation of high-energy electron–hole pair under UV-A light with wavelength of 385 nm or lower [30]. As mentioned above for bulk powder, TiO_2 NPs have the same mechanism based on the reactive oxygen species (ROS) generation with the advantage of being at nanoscale. This nanoscale nature implies an important increase of surface area-to-volume ratio that provides maximum contact with environment, water, and oxygen [31] and a minimal size, which can easily penetrate the cell wall and cell membrane, enabling the increase of the intracellular oxidative damage.

TiO_2 NPs are one of the most studied materials in antimicrobial applications due to its abilities, such as bactericidal photocatalytic activity, safety, and self-cleaning properties. The mechanism referred to in the antimicrobial action of TiO_2 is commonly associated with its ROS with high oxidative potentials produced under band-gap irradiation photo-induces charge in the presence of O_2 [30, 32-36]. ROS affect bacterial cells by different mechanisms leading to their death. Antimicrobial substances with broad spectrum activity against microorganisms (Gram-negative and Gram-positive bacteria and fungi) are of particular importance to overcome the MDR (multidrug resistance) generated by traditional antibiotic site-specific.

Self-cleaning effect of a textile material can be obtained by a photo-catalytically active (PCA) coating containing a photo-catalytically active TiO_2. Self-cleaning coatings react with and decompose organic compounds or pollutants, deposited on the textiles from the environment, under the effects of exposure to sunlight, particularly the ultraviolet radiation. The organic pollutants are decomposed to simple inorganic compounds such as CO_2 and H_2O and are removed under the effects of heat, wind and/or rain. The efficiency of the self-cleaning coating is dependent upon the photo-catalytic activity of TiO_2 catalyst, which is directly proportional to the total surface area of TiO_2 particles [37].

TiO_2 has been classified in humans and animals as biologically inert[38, 39], and is widely considered to be a "natural" material, which at least partially contributes to its relatively positive acceptance by the public. However, with the development of nanotechnologies, TiO_2 NPs, with numerous novel and useful properties, are increasingly manufactured and used. Therefore, increased human and environmental exposure can be expected, which has put TiO_2 NPs under toxicological scrutiny.

3. Possible Routes of Titanium Dioxide into the Environment and Humans

With attested high use of TiO_2 nanomaterials in various products, it is certain that some will get into the environment and subsequently into various organisms. The current realistic estimates of TiO_2 nanomaterials in air, water and soil are 1.5*10-3μgm-3, 0.7μgL-1 and 0.4μgkg-1 respectively[40], and these nanomaterials may enter the environment through many pathways, such as, emissions from production plants, disposal of wastes and used materials, accidental spills, and during transportation[41]. Research has also shown that TiO_2 nanomaterials get into the environment through wash offs and depositions, while TiO_2 nanomaterials in paints have been shown to leach out from the houses they are used on[40, 41]. TiO_2 nanomaterials from cosmetics and sunscreens wash off from bathing or simply cleaning them off. Treated wastewater sludge is also a route that gets TiO_2 nanomaterials into land[41]. All these may end up in natural water bodies or wastewater plants[1]. However, presence of TiO_2 nanomaterials in soil, water and atmosphere has been seen to be detrimental and toxic to bacteria, algae, nematodes, invertebrates, and humans[40].

TiO_2 nanomaterials have been shown to have been either ingested through contaminated particles, food or through direct dermal uptake in tissues of earthworms[41]. Although a healthy human skin prevents TiO_2 nanomaterials from entering it, an impaired skin (caused by injury, sunburn, extreme bathing, skin diseases) does not offer such protection; thereby, permitting these TiO_2 nanomaterials into the skin[6]. Another route of entry into humans is via inhalation, and the translocation of TiO_2 nanomaterials has also been reported in the brain of prenatally exposed mice, and possibly into humans, since blood-brain barriers are underdeveloped in the foetus[42].

The pathway for penetrating the cell is through the openings of the primary cell wall, consisting of a polysaccharidic-protein structure—which, depending on the pectic component, is porous[43]; the pore sizes range from 3.5 to 20.00 nm [44-46]and more often are around 5.00 nm. The progression to protoplasm is made possible by cell membrane-embedded protein carriers and ionic channels, or by membrane invagination (endocytosis), which forms vesicles around the passenger. The transport cell to cell is made dynamic by cytoplasmic channels, the plasmodesmata, which are 20.00 –50.00 nm in diameter at the midpoint and usually let inside small particles, around 3 nm [47], but the exclusion limits are subject to variations as endogenous proteins mediate crossing. Below the foliar epidermis, the photosynthetic palisade tissue (Figure 1) provides small intercellular spaces which, together with the cell walls, form the apoplastic pathway. Through the symplastic and apoplastic pathways, small particles can reach the photosynthate conducting system (phloem vessels), made up of living sieve-cells devoid of a nucleus and most organelles, while being connected to one another and to the surrounding tissues by wall sieve pores of 0.2–0.4 µm.

Underground, the roots are permeable only near the tips, where the epidermal cells extend out into hair roots (Figure 1); the remaining tracts (exodermis) are waterproofed by the suberin. Within the root the cortical apoplastic way is obstructed around the vascular system by a cell layer with radial walls impregnated by suberin (endodermis) (Figure 1), so the path to the vessels is through the tangential walls of the endodermis (symplastic way). However, the lateral roots enable an apoplastic path from the emergence zone up to the vessels [47]. Vessels consist of emptied cellular elements longitudinally connected to one another and to the surrounding cells with pits wider than 1 µm [48-50], so it is possible for small particles absorbed with the water to move passively within them.

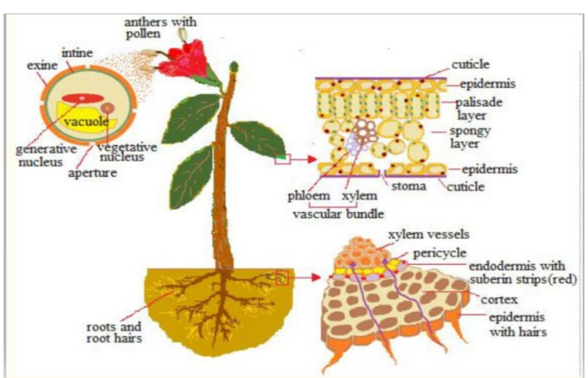

Fig. 1. Pathways by which TiO_2 nanomaterials are absorbed: pollen exine, cuticle, stomata, and root hairs[47]

The stem and its branches are wrapped by a tissue of suberized cells that replaces the epidermis; it is tiered by the radial growth of the stem. The annual and biennial plantlets do not grow radially, so their stems remain enveloped by epidermis provided with stomata.

4. Impact of Titanium Dioxide Nanomaterials on Organisms and Environment

A. *Micro-organisms*

TiO_2 nanomaterials have been shown to possess antimicrobial properties and its presence in the atmosphere will thus be toxic to many useful and harmful microbes. However, TiO_2 nanomaterials have been shown to be non-toxic to the viability and growth of C. metallidurans and Bacillus subtilis, a Gram-positive, catalase-positive bacterium, even after 6 h of exposure at 500mg/L[51-53]. At short exposure times, TiO_2 nanomaterials has zero or low toxicity towards ordinary heterotrophic organisms, ammonia oxidizing bacteria and thermophilic and mesophilic anaerobic bacteria in the wastewater treatment plant[54].

Lots of the TiO_2 nanomaterials in the environment ends up in the wastewater treatment plants. From those produced at the site of manufacture to those washed off from cosmetics, a large chunk ends in the wastewater treatment plants. TiO_2 nanomaterials concentration has been measured to be 185µgL-1 in wastewater treatment plant influent[55] and it has been shown that these NPs can also be found in sewage sludge[56].

Current environmentally relevant concentration of TiO_2 nanomaterials (1mg/L) has been shown to have no adverse effects on nitrogen and phosphorus removal and even at 50mg/L, TiO_2 nanomaterials did not influence wastewater nitrogen and phosphorus removal in long term exposure time and didn't deposit any Titanium ions[51]. At 50mg/L, it however caused serious inhibition to ammonia oxidation and therefore biological nitrogen removal after long term exposure which is suspected to be because of significantly decreased abundance of nitrifying bacteria (especially ammonia oxidizing bacteria)[51]. Surface sludge was not damaged by long term exposure to TiO_2 nanomaterials at 50mg/L[51]. E. coli, a Gram-negative, facultative anaerobic, rod-shaped, coliform bacterium also experienced a significant drop in survival (36% survival rate[57]) when exposed to a combination of UV light and TiO_2 NPs[21] and *Bacillus subtilis* had a survival rate of 71% when exposed to the same combination. Due to TiO_2's photocatalytic properties, a combination of UV light and TiO_2 NPs also significantly affected eukaryotic Leishmania parasites and inhibited their proliferation[20].

Neither low concentration TiO_2 NPs alone nor UV light alone significantly affected these organism's growth or survival but very high concentrations of ultrafine TiO_2 did inhibit the growth of bacteria; for example, E. coli reduced by 72% at 5g/L TiO_2 and *B. subtilis* experienced a similar reduction at a concentration of 1g/L TiO_2[12]. The toxicity to *Desmodesmus subspicatus*, a green alga, was dependent on the size and the crystalline form[58]. The antimicrobial effect of TiO_2 nanomaterials is dependent on several factors that include the particle size, exposure time, species of the organism, TiO_2 concentration and UV wavelength[57]. Table 1 presents some

Table 1
TiO_2 NPs against different microorganisms and their antimicrobial activities

Microorganism	Nanoparticles	Results
Methicillin-resistant *Staphylococcus aureus* [58]	Fe_3O_4-TiO_2 core/shell magnetic NPs	The survival ratio [%] of bacteria decreased from 82.40 to 7.13%.
Staphylococcus saprophyticus[59]	Fe_3O_4-TiO_2 core/shell magnetic NPs	The survival ratio [%] of bacteria decreased from 79.15 to 0.51%.
Streptococcus pyogenes [59]	Fe_3O_4-TiO_2 core/shell magnetic NPs	The survival ratio [%] of bacteria decreased from 82.87 to 4.45%.
Escherichia coli [60]	TiO_2 nanotubes ~ 20 nm	97.53% of reduction.
Staphylococcus aureus[60]	TiO_2 nanotubes ~ 20 nm	99.94% of reduction.
Bacillus subtilis [61]	TiO_2 NPs co-doped with silver (19–39 nm)	1% Ag-N-TiO_2 had the highest antibacterial activity with antibacterial diameter reduction of 22.8 mm.
Mycobacterium smegmatis [62]	Cu-doped TiO_2NPs ~20 nm	The percentage of inhibition was around 47%.
Pseudomonas aeruginosa [21]	TiO_2 NPs 10–25 nm	Although it was not completely euthanized, their survival was significantly inhibited.
Shewanella oneidensis MR-1 [62]	Cu-doped TiO_2 NPs ~20 nm	The percentage of inhibition was around 11%.

Table 2
Positive and negative effect of TiO2 NPs on various plant species

Nanoparticles	Plant species	Effects
TiO_2[67]	*Vigna radiata, Arabidopsisthaliana, Foenticum vulgare, Lemna minor, Triticum aestivum*	Enhanced germination, plant growth chlorophyll content

research including the antimicrobial capacity of TiO_2 NPs.

B. Terrestrial Plants

Due to the presence of dispersed and aggregated TiO_2 nanomaterials in the soil, air and water bodies, plants get to interact with them[41]. In a study of the effect of TiO_2 nanomaterials, corn (Zea mays) and jalapeno (Capsicum annuum) were exposed to three different concentrations of 300 mg/L, 600 mg/L, and 1000 mg/L of TiO_2 nanomaterials dissolved in water. The root mass of corn and jalapeno plants exposed to high levels of TiO_2 was lower than that of the control indicating inhibition of root growth. There was structural damage to the root epidermal cells in corn and jalapeno plants exposed to 1000 mg/L TiO_2 and the presence of titanium particles on the surface of both corn and jalapeno plant roots exposed to 1000 mg/L TiO_2 was indicated by EDS analyses. At exposure to the 1000 mg/L TiO_2 corn root cells became highly vacuolated but there was no presence of TiO_2 particles inside the cells while jalapeno showed clusters of particles within the root cells, but no vacuolization[63].

In studying the effect of TiO_2 nanomaterials on soyabean, plant growth was significantly impaired. In a comparison between the effects of TiO_2 and Fe_3O_4 NPs on soyabean, above ground, dry biomass was seen to be significantly affected by nanoparticle type with Fe_3O_4 NPs treated plants having significantly greater dry biomass than TiO_2 NPs treated plants. Root dry biomass was also marginally higher in plants treated with Fe_3O_4. Though leaf nitrogen content was unaffected by treatment, leaf carbon content was marginally higher in Fe_3O_4 treated as compared to TiO_2 treated plants[64].

The main objective of nanomaterials in agronomy is to promote plant protection, productivity and reduce nutrient losses [65]. They can also be used to reduce the toxicity of metals and increase crop productivity without high cost of energy [66]. The extensive uses of NPs promote seed germination, plant development. Table 2 shows the positive effect of TiO_2 on some plants.

C. Phylum Nematode

Some TiO_2 nanomaterials end up on land and in the soil, there is the possibility of interacting with various components of the soil. Sewage could contribute 120μg/kg[3] of TiO_2 nanomaterials into the soil per year and the content has been shown to range from 0.02 – 5.5% in some topsoil in Europe[41]. Soil invertebrates are an integral component of the soil ecosystem function as they help in decomposition and nutrient recycling and investigating the effects NPs have on them is important.

The behavior of NPs in soil is different from the dissolved phase because soil provides both a solid matrix and an aqueous phase. Aggregation rate of TiO_2 nanomaterials in soil is impacted positively by ionic strength, zeta potential and pH while dissolved organic matter and clay content affects it negatively. Long term stable TiO_2 nanomaterials lead to bioaccumulation because they are readily taken up if present in the soil pore water[41].

The toxicity of TiO_2 nanomaterials to nematodes in soil were studied through their exposure to food, soil, and water. LC50 dose for *Caenorhabditis elegans* exposed to TiO_2 nanomaterials for 24hrs was 80mg/L and the smaller the size of the TiO_2 nanomaterials, the more toxic it was[41]. Bulk TiO_2 became toxic at concentrations of >95.9mg/L while nano TiO_2 showed toxicity at >47.9mg/L. Both nano and micro TiO_2 also affect growth and reproduction in *C. elegans*[41].

TiO_2 nanomaterials had no effect on survival, weight change and glutathione S-transferase of *P. Scaber* exposed to 1000mg/ TiO_2 kg dry food. Exposure duration played an important role in toxicity of TiO_2 nanomaterials to nematodes. TiO_2 nanomaterials led to reproductive toxicity at 1000mg/kg dry natural soil in *E. fetida* but micron sized TiO_2 had no effect on its reproduction.

Although apoptosis was observed, bioaccumulation of TiO_2 nanomaterials was not observed in the earthworm *Lumbricus terrestris* when exposed through soil, food, and water because the nanomaterials could not pass the tissue barrier[41].

D. Phylum Chordata (With emphasis on Class Mammalia)

Humans are constantly exposed to several nanomaterials in their daily activities and TiO_2 nanomaterials is one of the most contacted daily. From manufacturing emissions, to cosmetics and sunscreen use, human cells interact with them. One of the most important properties of TiO_2 nanomaterials is their photocatalytic abilities and this same property is the reason for some of its potential hazards since it causes the production of ROS which are known to cause genetic damage and other adverse effects in living tissues[68]. These TiO_2 nanomaterials have been linked to some lung cancer in animals and thus it is important to know about their cyto- and genotoxicity in animals.

In a study of the cyto- and genotoxicity, DNA-adduct formation and generation of free radicals of TiO_2 nanomaterials on human bronchial epithelial cells (BEAS-2B) and human lung fibroblasts (IMR-90), it was discovered that IMR-90 were more sensitive regarding cyto- and genotoxicity caused by TiO_2 nanomaterials than BEAS-2B. TiO_2 nanomaterials did not induce DNA damage in both cell types nor did it induce cytotoxic effects in BEAS-2B cells up till a measure concentration of 50µg/cm^2 but caused a high level of DNA adduct formation and significant loss of cell viability in IMR-90 cells due to the generation of elevated amounts of free radicals which induced indirect genotoxicity[2].

As mentioned earlier, several properties determine the behavior of TiO_2 nanomaterials. Gurr *et al.,* (2005) studied the effect of size and form of TiO_2 nanomaterials on BEAS-2B cells4. The anatase-sized (10 and 20 nm) TiO_2 particles in the absence of photoactivation induced oxidative DNA damage, lipid peroxidation, and micronuclei formation, and increased hydrogen peroxide and nitric oxide production in the cells while anatase-sized (200 and >200 nm) particles did not induce oxidative stress in the absence of light irradiation; showing that smaller particles have a higher potential to induce oxidative damage. In terms of the form of the TiO_2 nanomaterials, the anatase form of TiO_2 was seen to be 1.5 times more photocatalytic than the rutile form. However, the rutile-sized 200nm particles induced hydrogen peroxide and oxidative DNA damage in the absence of light but the anatase-sized 200nm particles did not. Treatment of cells with a mixture of both forms also caused DNA damage[3]. Both types impaired cell function although anatase produced more damage. If the NPs are coated with polymer brush, they will not adhere to cell membranes and hence will not penetrate the cells thereby reducing ROS formation[60].

Kiss *et al.* (2008) used human skin transplanted in severe combined immunodeficient (SCID) mice to conduct in vivo penetration studies and to investigate the effect of TiO_2 NPs on various functional properties of epidermal and dermal human cells[6]. The reasons for the selection of mice are that they are small and inexpensive, have a widely varied diet, are easily maintained, can reproduce quickly and most importantly because they share a high degree of homology with humans. They discovered that TiO_2 particles do not penetrate through the stratum corneum of human skin transplants and that TiO_2 NPs were internalized by in vitro cultured fibroblasts and melanocytes but not by keratinocytes and sebocytes. TiO_2 exposure differentially affects proliferation and apoptosis in various human skin cells and decreased the expression of differentiation markers and cell adhesion molecules in keratinocytes. TiO_2 NPs elevate [Ca^{2+}] in both fibroblasts and melanocytes but not in keratinocytes and sebocytes.

Despite the various advantages of TiO_2, studies have shown that many TiO_2 nanomaterials end up in the environment, wastewater-collection systems, and subsequently biological systems[54]. TiO_2 nanomaterial concentration has been measured to be as high as 185µg/L in wastewater-treatment plants[54], and the assigned threshold value of TiO_2 nanomaterial at the American Conference of Governmental Industrial Hygienists (ACGIH) was 10mg/m^3 (total dust) for a normal 8h workday, and 40-hour work-week exposures can also occur by using products containing TiO_2 nanomaterial[2]. Although some studies have shown that the cytotoxicity of TiO_2 nanomaterials is negligible, compared to other particles[3], some studies have shown otherwise[1, 2, 5]. It is therefore, important to investigate TiO_2 NPs toxicity and environmental impact, due to their increased, use, large-scale production, and likelihood of increased environmental release[51].

The crystalline structure, particle size and coating can affect the surface charge, sedimentation, aggregation and thus toxicity of TiO_2 NPs [54, 69-72]. The previous in vitro and in vivo tests confirm the toxic effects of TiO_2 NPs on human body such as altered cell cycle, constriction of nuclear membranes and apoptosis [54, 69, 73-76]. Studies also showed that TiO_2 NPs can cause DNA damage [70], [77], [78] and interact with the epithelium of the small intestine responsible for absorption of nutrients. After exposure to TiO_2 NPs by various ways, mainly by inhalation, injection, skin contact and absorption in the alimentary tract, TiO_2 NPs can be found in different internal organs. In vivo tests revealed that after inhalation or oral exposure, TiO_2 NPs accumulate in, among other places, the lungs, alimentary tract, liver, heart, spleen, kidneys, and cardiac muscle [69, 79-81].

5. Possible Routes of Titanium Dioxide into the Environment and Humans

Because of their unique properties, TiO_2 nanomaterials are here to stay even though they have been seen to be toxic to various living things. Therefore, we have no choice than to proffer solutions to their toxicity. A good idea will be to modify their surface properties to suit various purposes. For instance, if dispersed in cosmetics and sunscreens, they should be coated in such a way that after washing these cosmetics off, the surface coating disappears and the already modified surface properties of the TiO_2 nanomaterials will allow them to aggregate instead of being dispersed. Aggregation will sure reduce their surface to volume ratio and allow them to behave in a similar manner to their micron sized counterparts which are biologically inert. Studies have shown that it is possible to graft a dense polymer coating on the TiO_2 nanomaterials that can trap electrons and suppress ROS production [82].

A similar aggregation technique may be tried in wastewater and atmospheric conditions where biologically inert materials which the TiO_2 nanomaterials have a strong attraction to may be dispersed so that these nanomaterials can aggregate on them and therefore sedimentation occurs. Bar screens, grit removal and primary settling are also possible techniques to remove these NPs from wastewater.

Careful handling of TiO_2 nanomaterials during production, transport, and disposal to avoid accidental spills or emissions may also prove to be critical to achieving a lower atmospheric level of these nanomaterials. These above-mentioned methods may just be what we need to control TiO_2 nanomaterials in the environment.

6. Conclusion and Recommendations

Nanomaterials have found applications in agricultural, industrial, and health sectors because of their unique combination of properties which include but not limited to their reactivity, mechanical and electrical properties. In the present review, the properties, synthesis, and applications of TiO_2 nanomaterials are discussed and the impact in wastewater and soil on microorganisms, plants, and humans as it relates to health, safety and environment was presented.

The unique properties of TiO_2 nanomaterials with photocatalytic abilities, ultraviolet light absorption and transparency make it a material for several future applications in consumer products, environmental, medical and semiconductor applications. There is also a great potential for it to be used as a novel route for administering nanoparticle-based diagnostics and/or therapeutic agents to cells if coated with some proteins such as nystatin. However further research needs to be done on its toxicity to various organisms. The current and past researchers have studied acute exposures and in vitro studies due to simplicity and low cost. The longest exposure was 48 hours, and all these experiments were done on immuno-suppressed organisms. These tests do not totally reflect what obtains in everyday life where immune and immuno-suppressed organisms are constantly exposed to these nanomaterials.

Nanomaterials are also known to transform after exposure to the environment due to overall environmental factors and may exhibit different properties from those of the original nanomaterials. These transformed ones are the most suitable for future research.

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