Chemical Analysis of Biochemically Toxic Metal Oxide Nanoparticles in Environmental Water

Abstract
This mini review focuses on studies recently reported concerning the chemical analysis of metal oxide nanoparticles in environmental water due to their biochemical toxicity. After an introduction to the most important chemical and physical characteristics of metal oxide nanoparticles, we review their latest use in scientific endeavors. Nowadays, these nanoparticles and their composites have attracted versatile applications based on many unique properties. Considerable research has been invested to improve the performance of materials prepared with nanoparticles. The diversity of these nanomaterials allows rapid development of novel catalysts, devices, sensors and technologies. Finally, we conclude with a perspective on the future direction of these nanoparticles in the controlled synthesis of nanohybrids.

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Synthesis

Metal (Ag, Au, Pd and Pt) and metal oxide (Al₂O₃, CdO, CeO₂, Co₃O₄, CuO, Fe₂O₃, Gd₂O₃, La₂O₃, MnO₂, NiO, Ru₂O₃, SiO₂, TiO₂, WO₃, and ZnO) nanoparticles (measuring 1-100 nm on their smallest axis) can be synthesized by biological, chemical, green, phytosynthetic, radiolytic and ultrasonic methods for numerous industrial and biomedical applications [1-7]. Metal in plants was extracted with H₂SO₄ to form sulfate which then reacted with OH⁻ to synthesize metallic oxide nanoparticles [8]. Simultaneous reduction/oxidation of metal ions and stabilization of the nanoparticles formed would be the key [9]. Several transition metal oxides (Co₃O₄, Cr₂O₃, CuO, NiO and ZnO) were synthesized under sunlight using water as a solvent [10]. Interestingly, they were able to catalytically remove over 80% of hazardous dyes such as alizarin red S and methylene blue in 3 hours for wastewater treatment.

Applications

Metal and metal oxide nanoparticles have mainly found applications that take advantage of their catalytic, electrochemical, enzymatic sorptive, scratch-resistant, sensing, size dependent surface thermodynamic, sorptive and thermophysical properties [11-22]. A global upsurge in antibiotic resistance has led to research in metal-oxide-based antimicrobial therapy [23]. Silver (Ag), copper (Cu), copper oxide (CuO) and zinc oxide (ZnO) exhibited antimicrobial properties against various pathogens in biofilms [24]. Ag and ZnO nanoparticles with antimicrobial action were applied in consumer and food packaging products [25]. Chitosan-capped copper oxide nanoleaves were blended with commercial paints for wood, steel and cement panels [26]. Their anti fouling behavior against three green and marine algae was 78%-92%. The toxicity of metal oxide nanoparticles could be divided into three categories: (1) the antibacterial effect of ZnO nanoparticles was due solely to the released Zn²⁺; (2) the antibacterial effect of CuO nanoparticles originated from both the released Cu²⁺ and the nanoparticles; and (3) the antibacterial effects of Fe₂O₃, Co₃O₄, Cr₂O₃ and NiO nanoparticles were caused by the nanoparticles themselves [27]. The antibacterial activity of ZnO/NiAl₂O₄, ZnO/CuAl₂O₄, ZnO/MgAl₂O₄ and ZnO/CoAl₂O₄ mixed oxides nanoparticles were demonstrated against Escherichia coli and Staphylococcus aureus bacteria species [28].

Mixed metal oxides in the nanoscale were of great interest for many energy-related research topics such as water splitting, fuel cells and battery technology [29]. Ceria (CeO₂) nanoparticles were used as a chemically stable catalyst for fuel oxidation and cracking of heavy petroleum residue to yield lighter fractions [30,31]. Nanoparticles with formula Ca₃Al₂SiO₇ and Ca₃Al₂O₇ were used as a heterogeneous catalyst for the transesterification of soybean oil with methanol to produce methyl esters for biodiesel [32]. Their emerging use enhanced the prospects of targeted drug delivery and improved the diagnostic ability of virus targeting agents [33]. Ag and TiO₂ nanoparticles hindered cotton/polyethylene terephthalate fabrics biodegradation in soil [34]. Polyethylene composites with ≤12 wt. % metal oxide nanoparticles were emerging materials for use in the insulation of extruded high-voltage cables [35]. CuO-ZnO nanoparticles and terephthalic acid were used to synthesize nanocomposite films that showed mechanical strength and brighter colors for packaging applications [36]. Significant degradation of E. coli bacteria was observed on ZnO-Cds-Ag photocatalyst under UV and visible light irradiation [37]. Metal oxide nanoparticle resists recently emerged as next generation photoresist materials which exhibited promising performance to pattern 20-nm features for extreme ultraviolet lithography [38]. Composites of metal oxide and metal nanoparticles with bacterial cellulose nanoribbons allowed targeting of many catalysis, photocatalysis, electrochemical device and sensor applications [39]. High concentrations of NiO nanoparticles inhibited the microbial enzymatic activity of activated sludge [40]. The influence of Ag₂O and TiO₂ nanoparticles on the reduction of chemical oxygen demand in activated sludge was observed after 180 days [41]. A promising new generation of flat-panel solar thermal collectors used metal oxide nanoparticles in liquid-based nanofluids to enhance the thermal absorption efficiency [42]. There was an increase in the thermal decomposition of propellants in the presence of transition metal oxide nanoparticles [43].

Unique Properties

Fast adsorption of phosphate was achieved only 45 min by iron oxide nanoparticles in a wide range of pH 1-11 [44]. Cetyltrimethylammonium bromide (CTAB) as a stabilizer was efficient in removing phosphate from 71% to 97%. The adsorption capacity of phosphate increased when the temperature or initial phosphate concentration increased and decreased with an increase in pH. Adsorption followed the pseudo-second-order kinetics model and the equilibrium data fitted well to the Langmuir isotherm. Thermodynamic data confirmed the spontaneous and endothermic nature of the adsorption process. The adsorption of phosphate using CTAB-modified iron oxide nanoparticles was mainly associated with the inner-sphere complexing mechanism and electrostatic attraction. Lauryl gallate (LG) showed strong adsorption on Ag and MnO₂ particles [45]. The adsorption mechanism involved complexion of metal atoms on the particle surface with phenolic OH group of LG.

TiO₂ nanoparticles have a specific surface reactivity and bind bidentate ligands from the environment. Carbon nanotube (CNT) growth has been demonstrated recently on a number of nonmetallic semiconducting (oxidized Si nanocrystals) and metal oxide nanoparticles using a microwave plasma enhanced chemical vapor deposition method [46]. A simple method of functionalization with epoxy silane was used to prepare fluorescent-labelled SiO₂ nanoparticles directly in aqueous phase [47]. The amount of fluorescent label per particle remained constant regardless of size, which facilitated the measurement of number-based concentrations. Interaction of metal oxide nanoparticles with aquatic contaminants has a significant impact on their environmental fate and transformation [48].

Biochemical Toxicity

Industrial, commercial and agricultural applications of these nanoparticles could result in their accumulation in soil, threatening higher terrestrial plants. Unfortunately, metal and metal oxide nanoparticles may have negative effects on the growth and yield of food crops [49]. The biochemical and
physiological responses of plants to stress imposed by metal oxide nanoparticles have been reviewed [50].

Toxic effects of metal oxide nanoparticles were observed in a wide range of organisms [51]. Nanoparticles could be without cytotoxicity at concentrations ≤ 50 µg/ml; however, some metal oxide particles caused subtle concentration-related changes in spontaneous and/or GABA receptor-mediated neuronal activity in vitro even when cytotoxicity is absent [52]. Reactive oxygen species production and lactate dehydrogenase release demonstrated that CuO nanoparticles induced toxicity towards microorganisms and destroyed the integrity of microbial cytomembrane [53].

Increased lysosomal membrane permeability, DNA damage, and histopathological effects were induced by TiO2 nanoparticles in scallops after aqueous exposure [54]. ZnO nanoparticles elevated Zn levels in the digestive gland of mussels [55]. They also induced specifically a strong decrease in the mitochondrial function and an increase in the methyglyoxal-associated DNA damage in macrophages [56]. Despite no apparent accumulation, ZnO nanoparticles exposure to common carp disturbed the fish homeostasis by affecting proteins of the hematological and the immune systems [57]. Zebrafish exposed to CdO nanoparticles prepared by calcination of Cd-citrate coordination polymer expressed reduced toxicity as judged by lower oxidative stress levels, rescue of liver carboxylesterases, and reduction in metallothionein activity compared to CdO nanoparticles prepared by calcination of Cd(OH)2 [58].

It has been experimentally shown that the introduction of Al2O3, CeO2, TiO2, and ZnO nanoparticles to laboratory mice changed some specific hematological and biochemical blood parameters [59]. A mixture of CeO2 and ZnO nanoparticles exerted a higher combined cytotoxicity to environmental organisms than those from the individual nanoparticles [60]. The release of Zn2+ and Ni2+ aggravated the allergic reaction to inhaled ovalbumin in mice [61]. Existing data on the toxicity of inhaled nanomaterials in animal models are sparse in comparison to the number of potential factors that may affect toxicity. The acute (24 hours) and persistent (13 weeks) effects in the airways after a single exposure to metal oxide nanoparticles were studied using a murine inhalation model [62]. Mice were exposed 60 min to aerosols of either ZnO, TiO2, Al2O3, or CeO2. The ranking of potency regarding induction of acute lung inflammation was Al2O3 > TiO2 > CeO2 ≪ ZnO. ZnO caused a significant toxic effect in the airways while TiO2 gave rise to DNA-strand break. Al2O3, SiO2, and ZnO nanoparticles on red blood cells of Wistar rats caused transformation of discocytes into echinocytes and spheroocytes [63]. Microviscosity change began prior to cell shape alteration.

Aluminum oxide (Al2O3) nanoparticles were capable of triggering up-regulation of genes related to the cell death in a human A549 lung adenocarcinoma cell line [64]. The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazoliumbromide and lactate dehydrogenase assays showed that CuO nanoparticles (5-15 µg/mL) exert cytotoxicity in A549 cells in a dose-dependent manner [65]. DNA adsorption of metal oxide nanoparticles has been confirmed [66]. Salt concentration, pH, DNA sequence and length affected DNA adsorption. The adsorption mechanism was found to be through the alamarBlue® assay, genotoxicity tests using two human cell lines (A549 alveolar epithelial cells and lymphoblastoid TK6 cells), and DNA strand break measurement with the comet assay implied that CeO2, TiO2, and ZnO — whether cytotoxic or not — are genotoxic [67]. The in vitro cytotoxicity and genotoxicity of Al2O3, Co3O4, Fe2O3 and SiO2 nanoparticles on human lymphocytes were compared [68]. The Co3O4 nanoparticles showed decrease in cellular viability and increase in cell membrane damage followed by Fe2O3, SiO2 and Al2O3 nanoparticles in a dose-dependent manner after 24 h of exposure to human lymphocytes.

Occupational Hazards

The presence of metal and metal oxide nanoparticles in the occupational environment, not only in nano-industry but also in some long-existing technologies as well, necessitates careful control of hazardous exposures [69]. For humans, exposure through the skin contact, inhalation, and oral uptake are most common. The ubiquitous use of metal oxide nanoparticles — intentionally engineered to express novel properties - in semiconductor fabrication poses unique issues for protecting worker health and safety [70]. A combination of filter-based air sampling and direct-reading instruments was used to identify, characterize, and quantify the potential for worker inhalation exposure to airborne Al2O3, CeO2 and amorphous SiO2 nanoparticles associated with the chemical mechanical wafer polishing process. Nanoparticles can potentially induce toxicity in the lung by activating the main mitogen-activated protein kinases and the nuclear factor NFkB to release inflammatory cytokines [71]. Four metal oxide nanoparticles (Fe2O3, Fe3O4, MnFe2O4 and CrOOH) are representative of those found in the welder’s lungs [72]. All but Fe2O3 nanoparticles induced the development of peribronchiolar, perivascular and alveolar fibrosis, together with interstitial inflammation. Inhaled CdO nanoparticles not only accumulated in lungs but they were also transported to other organs causing serious damage at tissue as well as cellular level [73]. Small airway epithelial cells engulfed CoO and La2O3 nanoparticles; CoO nanoparticles produced more superoxide radicals and caused greater stimulation of total tyrosine and threonine phosphorylation [74]. Inhalation exposure to WO3 nanoparticles induced cytotoxicity and lung injury via pyroptotic cell death pathway caused by activation of inflammasome caspase-1 [75]. Meta-analysis-based risk models have been developed with the machine-learning technique, random forests, to determine the relative contribution of different physical and chemical attributes on observed toxicity [76].

Food Safety

Oral uptake is probably the most important way for metal oxide nanoparticles to enter the body due to the high amounts of nanoparticles in food and the large absorption area of the gastrointestinal tract [77]. These nanoparticles can penetrate biological barriers at a high translocation rate and may distribute differently in the body according to size. On gastrointestinal cells, Ag nanoparticles damage bacteria at lower concentrations than enterocytes, while the opposite is true for ZnO nanoparticles [78]. TiO2 nanoparticles are commonly present in food additives and have been associated with potential adverse effects
on health. The interactions between TiO$_2$ nanoparticles and flavonoids (i.e. apigenin, luteolin, fisetin, kaempferol, quercetin, myricetin, and baicalin) to form complexes were subjected to Raman spectroscopic analysis of their molecular interaction [79]. Phenolic groups in the flavonoids played pivotal roles in the interaction between flavonoids and TiO$_2$ nanoparticles. A difference in the number and positions of phenolic groups could contribute to distinctive spectral peaks for different complexes.

Environmental Waters

Chemical transformation of metal oxide nanoparticles is exemplified by ZnO – carbonate or phosphate in solution can reduce ZnO nanoparticle dissolution due to the formation of insoluble carbonate and phosphate species on the nanoparticle surfaces [80]. Nanoparticle binding with organic ligands in natural waters is important to understand their environmental behavior and fate [81]. The effects of various aquatic contaminants on the transformation, transport kinetics and toxicity of metal oxide nanoparticle have been reviewed [82]. The presence of contaminants decrease bioavailability through hetero-aggregation, sorption, or complexation upon interaction with metal oxide nanoparticles. Water chemistry influenced the aggregation, sedimentation and dissolution of ZnO nanoparticles [83]. Stabilized nanoparticles aggregated and precipitated when the pH got close to their point of zero charge. Counter-ions neutralized the surface charge of nanoparticles and promoted their destabilization. However, a high concentration of counter-ion (SO$_4^{2−}$ > 10 meq/L) made the nanoparticles more stable by inverting the surface potential. A set of theoretical descriptors for modeling or grouping of metal oxide nanoparticle properties and biological activity was developed based on the force-field calculation of the potential energies of whole nanoparticles [84]. Grouping by principle component analysis was found to be in good accordance with the algal growth inhibition data.

Analysis of Metal Oxide Nanoparticles

Analysis of metal oxide nanoparticles and their released metal ions is essential for understanding their biological toxicity and environmental impact. Nanoparticles can be characterized using various spectral, microscopic and electrochemical techniques like X-ray photoelectron spectroscopy (XPS), X-ray diffraction (XRD), energy dispersive X-ray spectroscopy (EDS), transmission electron microscopy (TEM), scanning electron microscopy (SEM), selective area electron diffraction (SAED), electron paramagnetic resonance (EPR), Fourier transform infrared spectroscopy (FTIR), Raman spectroscopy, gravimetric analyses (TGA and DSC), photoluminescence (PL), ultraviolet-visible (UV-vis) spectroscopy, and electrocatalysis [85-93]. TEM provides ultrahigh resolution but involves cumbersome sample preparation rendering the technique incompatible with live cell imaging. Reflected light imaging, with X-Y resolution of 115 nm, provided an alternative non-destructive label-free technique well suited to the visualization of nanoparticles uptake within cells [94]. Although analytical techniques (using microelectrode arrays) are available to detect nanoparticles in pure systems, they are not specific enough to quantify engineered nanoparticles in complex environmental matrices comprising soil, sediment, or sewage sludge [95].

Enhanced darkfield microscopy (EDFM) was used as to visualize industrial metal oxide nanoparticles (silica, ceria, or alumina) in multiple tissue types following inhalation in rats mimicking occupational exposures. Advantages of EDFM over electron microscopy include reduced cost, time, and ease of sample preparation and operation. Following 6-hour inhalation exposures at three concentrations (3.5-34 mg/m$^3$), lungs and secondary organs were harvested at 24 hours or 7 days post-exposure and prepared for brightfield (BF) microscopy and EDFM. NPs were visualized within the lung and associated lymphatic tissues and in major organs of excretion (liver, spleen, kidney). EDFM also revealed NPs within pulmonary blood vessels and localization within specific regions in liver and kidney, indicating pathways of excretion [96]. Confirmation of the composition, distribution, and relative abundance of inhaled NPs can be pursued by combining EDFM with hyperspectral imaging (HSI) and mapping. CytoViva® enhanced darkfield hyperspectral microscopy is now being used extensively for optical observation and hyperspectral characterization of nanomaterials in-situ, e.g., mapping Fe$_2$O$_3$ nanoparticle aggregates in stained tissue [97]. *Ex-vivo* confirmation of the presence of nanoparticles in targeted tissue is critical in determining the efficacy of nanotheranostic therapies. An important element in this confirmation process is the ability to observe nanoparticle localization quickly and accurately across a large number of tissue samples.

Inductively coupled plasma mass spectrometry (ICP-MS) was used to determine the release of ZnO nanoparticles from antimicrobial food contact materials [98]. Single-particle inductively coupled plasma mass spectrometry (SP-ICP-MS) has emerged as a reliable tool that can both count metal-containing nanoparticles and measure their mass. Sizing is allowed if their shape, density, and composition are known. A priori, the following information related to specific elements can be obtained: (i) qualitative information about the presence of particulate and dissolved forms, (ii) quantitative information as particle number as well as mass concentrations, and (iii) characterization information about the mass of elements per particle and particle size [99]. The presence of natural organic matter in the nanoparticle suspensions led to a decreased adsorptive loss in both the sample containers and the sample introduction system, suggesting that SP-ICP-MS may nonetheless be appropriate for NP analysis in environmental matrices [100]. Coupling of an ion-exchange resin to the SP-ICP-MS led to more accurate determinations of the La$_2$O$_3$ nanoparticle size distribution. A novel approach, based on flow injection analysis coupled to ICPMS, does not require a determination of the transport efficiency and the sample uptake rate for the accurate measurement of particle mass [101]. A method for the sizing and quantification of CeO$_2$ nanoparticles by coupling ICP-MS to two modalities of asymmetric flow and hollow fiber flow field flow fractionation [1]. Citrate-stabilized Ag and Au nanoparticles were detected at the pmol/L level in aqueous mixture without previous separation by using basic fuchsin as molecular probe [103]. The method was validated by application to spiked drinking water. Another acid-base indicator, rosolic acid, permitted the semi-quantitative detection of mixtures containing two different kinds of silver nanoparticles. The proposed strategy represents a fast, simple and cost-effective methodology to determine mixed metal nanomaterials, being sensitive to metal identity and ligands on
the metal surface. Alongside field flow fractionation (FFF), SP-ICP-MS has allowed for the accurate measurement of size and particle number concentrations of mixed Ag and Au nanoparticles and a bimetallic Au@Ag core-shell structure [104]. Metal oxide nanoparticles can transform under environmental conditions, and the occurrence of natural particles of similar composition can bring additional challenges.

Size exclusion chromatography (SEC) was coupled with ICP-MS for speciation of metal oxide (NiO, CoO, ZnO, CuO, and CeO$_2$) nanoparticles and their released metal ions (M$^{n+}$). By using a 1000Å pore size silica column and an acetate buffer (pH 7.0, 10 mM) containing 10 mM sodium dodecyl sulfate as a mobile phase, M$^{n+}$ and nanoparticles with sizes smaller than the column pore size were baseline separated; nanoparticles with sizes larger than the exclusion limit were filtered off by the column [105]. The high recovery of M$^{n+}$ from the SEC column ensured their accurate quantification by SEC-ICP-MS. The quantification of metal oxide nanoparticles was obtained by subtracting the M$^{n+}$ content from the total metal content (which was determined with ICP-MS after digestion without SEC separation). Detection limits were as low as 0.016-0.390 µg/L for both M$^{n+}$ and metal oxide nanoparticles.

A new certified reference material for quality control of nanoparticle size analysis methods has been developed by the Institute for Reference Materials and Measurements of the European Commission’s Joint Research Centre. The material, ERM-FD102, consists of an aqueous suspension of a mixture of silica nanoparticle populations of distinct particle size and origin [106]. The characterization relied on an interlaboratory comparison study in which a variety of techniques were used for particle size analysis including atomic force microscopy (AFM), asymmetrical flow field-flow fractionation (AF4), centrifugal liquid sedimentation (CLS), dynamic light scattering (DLS), particle tracking analysis (PTA), SEM, and TEM.

Capillary Electrophoresis

Capillary electrophoresis (CE) research has come a long way since the technique was discovered in the 1980's. CE is a separation technique well suited for the analysis of environmental samples due to its high separation efficiency [107]. Quantitative determination of metal oxide nanoparticles in water by CE analysis with UV detection is intuitively direct. Moreover, changes observed in CE migration time and UV peak area could identify the analyte to be nanoparticles but not solute species. It is of critical importance to consider their stability and tendency to aggregate as a consequence of their intrinsic surface chemistry interacting with the complex environmental water matrices. One plausible approach lies in the proper choice of a background electrolyte (BGE) and the addition of a surfactant to break down any interaction, aggregation, agglomeration or sedimentation.

CE-UV characterization and detection of colloidal SiO$_2$ nanoparticles in water is technically simple and operationally cost effective. Once all parameters such as the composition and concentration of the BGE, the injection time, the applied voltage, and the use of surfactants are set, UV detection at different wavelengths will enable optimization of the analytical selectivity. Unfortunately, inadequate sensitivity is often encountered.

Coating of the nanoparticles with polyhydroxypropyl methacrylate (PHPMA) and polydopamine overnight gained only a moderate enhancement of the UV detection sensitivity by 12 folds [108]. The need for thicker polymer coatings to attain higher sensitivity would require longer time. Alternatively, binding of hydroxypropyl methacrylate (HPMA) with SiO$_2$ nanoparticles produced a higher absorbance for more sensitive detection by CE-UV [109]. On the contrary, binding with TiO$_2$ nanoparticles could not take place in 10 mM Na$_2$HPO$_4$, resulting in no change of their CE-UV detection sensitivity. Chitosan coating of SiO$_2$ nanoparticles was more efficient, producing a significant increase in SiO$_2$ hydrodynamic diameter. However, CE-UV analysis of chitosan-SiO$_2$ nanoparticles failed due to interaction of chitosan with the capillary wall. Subsequently, PHPMA binding with chitosan-SiO$_2$ nanoparticles facilitated the CE-UV analysis without any disturbance. A total enhancement of 50 folds in SiO$_2$ detection sensitivity was attained. This method is simple, rapid and selective for SiO$_2$ in 10 mM Na$_2$HPO$_4$. Moreover, it is environment friendly as no chemical initiator was required. Adsorption of DNA, polyethylene glycol (PEG) and Triton X-100 onto Al$_2$O$_3$, SiO$_2$, TiO$_2$, and ZnO nanoparticles reached equilibrium within 3 hours. All adsorbates were selective for TiO$_2$ nanoparticles in 100 mM tris(hydroxymethyl)aminomethane (Tris), enhancing their UV detection sensitivity by many folds in CE analysis [110]. The reaction medium was the most influencing factor controlling the selectivity of various adsorbates towards TiO$_2$ nanoparticles. Single-stranded DNA adsorbed onto TiO$_2$ nanoparticles more than the other adsorbates, producing an enhancement of 13 folds in UV detection sensitivity. The total surface area of disaggregated nanoparticles was hence availed, as well as their chemical functionality. Thiol molecular adsorbates, such as cysteine (Cys) and dithiothreitol (DTT), have been found to be selective for ZnO in the presence of Al$_2$O$_3$, CeO$_2$, SiO$_2$ and TiO$_2$ nanoparticles in 10 mM Na$_2$HPO$_4$ [111]. Adsorption equilibrium was reached within 10 min for Cys but 90 min for DTT to speed up the analysis. A monolayer of adsorbate molecules around each ZnO nanoparticle both enhanced the UV light absorbance (by 19 and 27 folds respectively) and rendered a long colloidal stability. Cenrifugation of the transparent Cys-ZnO dispersion showed no precipitation of these nanoparticles, allowing facile separation from any precipitated Al$_2$O$_3$, CeO$_2$, SiO$_2$ and TiO$_2$ nanoparticles. Nonetheless, those enhancements in detection sensitivity were still not sufficient for the quantitative determination of nanoparticles at environmentally relevant concentrations.

Now that the feasibility is demonstrated for the above physicochemical approach, various fluorescent probes are worth exploring to further enhance the detection sensitivity. A cationic inorganic dye, tris(2,2’-bipyridyl)dichlororuthenium(II) hexahydrate can be employed for laser induced fluorescence (LIF) detection of SiO$_2$ nanoparticles in CE analysis. A DNA-specific probe, 4’,6-diamidino-2-phenylindole, can form a fluorescent complex by attaching to the minor groove of A-T rich DNA sequences for the detection of DNA-stabilized TiO$_2$ nanoparticles by CE-LIF. Graphene quantum dots (GQDs), the zero-dimensional form of graphene with diameters below 100 nm, offer tunable optoelectronic properties directly associated...
with quantum confinement. GQDs are easily prepared in aqueous solution via hydrothermal processing of citric acid at 280°C. They can be functionalized with cysteine (Cys) through an amidation reaction at a basic pH [112]. Cys-GQDs can be exploited as a fluorescent probe for the sensitive detection of ZnO nanoparticles in water using CE-LIF. Fluorescent labelling, however, suffers from photobleaching, poor bioconjugation and alteration of nanoparticle surfaces. With the successful development of these proposed strategies in improving the detection sensitivity for metal oxide nanoparticles, they must next be validated using certified reference materials to assure their applicability for the quantitative determination of metal oxide nanoparticles in real-world water matrices.

Future Prospects

Finally, nanohybrids composed of noble metals and metal oxides have received considerable attention for applications in solar energy conversion, photocatalytic degradation of organic pollutants, photocatalytic hydrogen generation, and photocatalytic CO₂ reduction [113]. Composites based on metal-organic frameworks (MOFs) are an emerging class of porous materials that have been shown to possess unique functional properties. Nanoparticles@MOF composites combine the tailorable porosity of MOFs with the versatile functionality of metal or metal oxide nanoparticles. A wide range of nanoparticles@MOFs have been synthesized and their performance characteristics assessed in molecular adsorption and separation, catalysis, sensing, optics, sequestration of pollutants, drug delivery, and renewable energy [114].

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