# Theoretical study on the Multiscale Quantum–Molecular Modelling of Ecotoxicological Risks in Metal Oxide Nanomaterials.

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**Abstract: -** The Metal oxide nanomaterials (MONMs) are widespread applications in industries such as electronics, catalysis, and biomedicine have prompted significant concerns regarding their ecotoxicological impacts. The advanced quantum mechanical approaches, including density functional theory (DFT) and molecular dynamics (MD) simulations, are used to assess the environmental impacts and toxicity mechanisms of MONMs. In the modelling of electronic structure, surface reactivity, and intermolecular interactions of MONMs with biological and environmental systems, we are studying their behavior in aquatic and terrestrial ecosystems. The parameters, such as particle size, surface functionalization, and chemical composition, are analyzed to understand their influence on ecotoxicity and explore how electronic properties, such as band gap and charge distribution, govern the reactivity of MONMs with biomolecules and environmental media, potentially leading to oxidative stress or cellular damage. MD simulations give insights into the aggregation, dissolution, and bioaccumulation tendencies of MONMs under varying environmental conditions, such as the surface modifications in mitigating toxicity, and identify critical physicochemical properties that drive ecological risks. This work establishes a predictive structure for evaluating the safety of MONMs, offering a molecular-level understanding of their environmental fate, integrating quantum mechanical insights with ecotoxicological assessments, and developing safer nanomaterials, and informing regulatory composition to minimize ecological harm with their potential environmental impacts.

**Keywords:** Metal oxide nanomaterials(MONMs), Ecotoxicology, Quantum Mechanics, Molecular dynamics, Environmental risk, Surface reactivity, Nanoparticle toxicity.

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**1. Introduction:** Nanotechnology has emerged as a transformative field in the 21st century, revolutionizing industries such as medicine, electronics, catalysis, and energy storage. Among the broad class of nanomaterials, metal oxide nanomaterials (MONMs) such as titanium dioxide ($TiO_2$), zinc oxide (ZnO), cerium oxide ($CeO_2$), and iron oxide ($Fe_2O_3$) are among the most extensively utilized due to their unique physicochemical properties, including high surface-to-volume ratio, tunable band gap, redox activity, and surface reactivity [1,2]. These properties make MONMs essential in photocatalysis, environmental remediation, biomedical imaging, and drug delivery.

However, the extensive production and use of MONMs have raised serious environmental concerns, particularly regarding their potential toxicity in both aquatic and terrestrial ecosystems. We are studying and demonstrating that nanoparticles can interact with cellular systems, disrupt metabolic pathways to induce oxidative stress in microorganisms, plants, and animals [3, 4]. Their small size allows them to penetrate biological membranes, while their surface properties determine their reactivity with biomolecules, making them both useful and hazardous.

The growing concern over nanotoxicology has prompted the integration of advanced computational approaches such as Density Functional Theory (DFT) and Molecular Dynamics (MD) simulations. These methods give insights into electronic structure, intermolecular interactions, aggregation tendencies, and dissolution behaviour of MONMs, which are difficult to fully assess using experimental methods alone [5]. These mechanisms at the quantum and molecular level are essential for predicting long-term ecological risks and developing safe-by-design nanomaterials.

## 2. Literature Review

**A. Applications and Environmental Release of MONMs :** MONMs are widely applied in electronics, cosmetics, catalysis, and environmental remediation. Titanium dioxide nanoparticles, for instance, are used in sunscreens and photocatalytic water treatment systems due to their UV absorption capability [6]. Zinc oxide nanoparticles are incorporated in paints, sensors, and food packaging materials. However, their release during production, usage, and disposal contributes significantly to their environmental accumulation [7].Wastewater treatment plants, for instance, are a major pathway for MONMs entering aquatic ecosystems, where they undergo aggregation, sedimentation, or interaction with natural organic matter (NOM) [8].

**B. Ecotoxicological Impacts of MONMs :** The toxicological behaviour of MONMs is determined by size, shape, surface chemistry, and solubility. Studies show that ZnO nanoparticles readily dissolve in water, releasing $Zn^{2+}$ ions that cause oxidative stress in algae and fish [9]. $TiO_2$ nanoparticles, though less soluble, can generate reactive oxygen species (ROS) under UV irradiation, leading to DNA damage and lipid peroxidation [10].

The equation representing ROS generation from photoexcited MONMs is:

i. Pair generation

$$\mathrm{MONM} + h\nu \rightarrow \mathrm{MONM}(e^{-}_{\mathrm{CB}} + h^{+}_{\mathrm{VB}})$$

ii. Hole oxidation (surface)

$$h_{\mathrm{VB}}^{+} + \mathrm{H_2O}_{(ads)} \rightarrow \cdot\,\mathrm{OH}_{(ads)} + \mathrm{H}^{+}$$

$$\text{or,} \quad h_{\mathrm{VB}}^{+} + \mathrm{OH}_{(ads)}^{-} \rightarrow \cdot\,\mathrm{OH}_{(ads)}$$

iii. Electron reduction of oxygen (surface)

$$e_{\mathrm{CB}}^{-} + \mathrm{O}_{2(ads)} \rightarrow \mathrm{O}_{2(ads)}^{\cdot -}$$

Where: $h\nu$ = photon energy, $e_{CB}^{-}$ = excited electron in conduction band, $h_{VB}^{+}$ = hole in valence band, $\cdot OH$ and $O_2^{\cdot -}$ = ROS causing oxidative stress. This mechanism explains how nanoparticles induce oxidative stress and cellular toxicity.

**C. Impacts of Computational Approaches :** The complexity of MONMs' interactions in biological systems has encouraged the adoption of computational nanotoxicology.

i. Density Functional Theory (DFT): Used to model band structure, charge distribution, and adsorption of biomolecules on MONM surfaces [11].

ii. Molecular Dynamics (MD) Simulations: Explore nanoparticle aggregation, protein corona formation, and transport across lipid bilayers [12].

For example, DFT studies show that surface modifications with functional groups such as COOH or –OH can reduce the reactivity of nanoparticles by passivating active sites [13]. Similarly, MD simulations predict how MONMs aggregate in saline environments, influencing their bioavailability.

## 3. Methodology

### A. Computational Framework

The methodology in this study involves a two-tiered computational framework:

i. Electronic Structure Calculations using Density Functional Theory (DFT)

ii. Dynamic Behavior and Bio-Interaction Studies using Molecular Dynamics (MD) Simulations

This integrated approach allows us to assess both the intrinsic electronic properties of MONMs and their extrinsic interactions in environmental media.

(i) **Density Functional Theory (DFT) Modelling:-** DFT is employed to model the band structure, density of states (DOS), charge distribution, and adsorption energies of MONMs. The fundamental principle of DFT is solving the many-body Schrödinger equation for an interacting system of electrons under an external potential:

$$\hat{H}\Psi = E\Psi \ldots (1)$$

where: $\hat{H}$ is the Hamiltonian operator, $\Psi$ is the many-electron wavefunction, and E is the total energy of the system.

In DFT, the Kohn-Sham equations are solved:

$$\left[-\frac{\hbar^2}{2m}\nabla^2 + V_{ext}(r) + V_H(r) + V_{XC}(r)\right]\psi_i(r) = \epsilon_i\psi_i(r) \text{ ………….. (2)}$$

where: $V_{ext}$ = external potential from nuclei, $V_H(r)$ = Hartree potential, $V_{XC}(r)$ = exchange-correlation potential, $\epsilon_i$ = eigenvalue corresponding to orbital $\psi_i$.

Using DFT, we calculate:

i. Band gap ($E_g$ ) of MONMs,

ii. Adsorption energy ($E_{ads}$) of biomolecules or environmental ligands:

$$E_{ads} = E_{NP+\,Ligand} - \left(E_{NP} + E_{Ligand}\right) \text{ ………………..… (3)}$$

A negative $E_{ads}$ indicates a favorable interaction, which can suggest potential toxicity due to strong biomolecular binding [15].

**(i) Molecular Dynamics (MD) Simulations:-** The DFT provides static electronic insights, MD simulations model dynamic environmental interactions of MONMs. Newton's second law determines the time evolution of atomic positions:

$$m_i\frac{d^2r_i}{dt^2} = F_i \text{ ……………………………………(4)}$$

where: $m_i$ = mass of particle, $r_i$= position of particle, $F_i$ = interatomic force, usually derived from potential energy functions.

In classical MD, interactions are modelled using potential functions such as the Lennard-Jones potential:

$$V(r) = 4\epsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right] \text{ ………………… (5)}$$

where: $\epsilon$ = depth of potential well (interaction strength), σ = distance at which potential is zero, r = distance between particles.

For charged MONMs, electrostatic interactions are modelled via Coulomb's law:

$$V_{Coul}\,(r) = \frac{1}{4\pi\epsilon_0}\cdot\frac{q_1q_2}{r} \text{ ……………………… (6)}$$

This helps evaluate aggregation, protein corona formation, and bioaccumulation tendencies.

**B. Ecotoxicological Structure :** We are calculating those models from ecological impacts with the help of computational results. The relationship between MONM concentration and observed toxicity can be represented by a sigmoidal Hill equation:

$$E(C) = \frac{E_{max}\cdot C^n}{EC_{50}^n + C^n} \text{ ………………….. (7)}$$

where: $E(C)$ = biological effect at concentration, $E_{max}$ = maximum effect, $EC_{50}^{n}$ = concentration at which 50% effect occurs, $C^{n}$ = Hill coefficient (cooperativity factor).

This model is used to quantify lethal concentration (LC50) or effective concentration (EC50) for aquatic organisms exposed to MONMs [16].

### C. Observations

i. Titanium Dioxide ($TiO_2$): Focus on ROS generation under UV exposure.
ii. Zinc Oxide (ZnO): Focus on ion release ($Zn^{2+}$ dissolution) and toxicity to algae.
iii. Cerium Oxide ($CeO_2$): Known for dual role: antioxidant ($Ce^{3+}/Ce^{4+}$ redox cycling) vs toxicity under certain pH conditions.
iv. Iron Oxide ($Fe_2O_3$): Studied for aggregation and bioaccumulation in sediments.

Each case study integrates DFT-calculated reactivity, MD-predicted aggregation, and toxicity dose-response curves.

### D. Surface Functionalization

The mitigation strategy is surface modification of MONMs, for instance:

i. PEGylation (coating with polyethylene glycol)
ii. Carboxylation (–COOH groups)
iii. Salinization

Computational modelling shows that such modifications reduce surface reactivity by altering the electrostatic potential distribution. This can be visualized using DFT-derived electrostatic potential maps.

### E. Operation Diagram

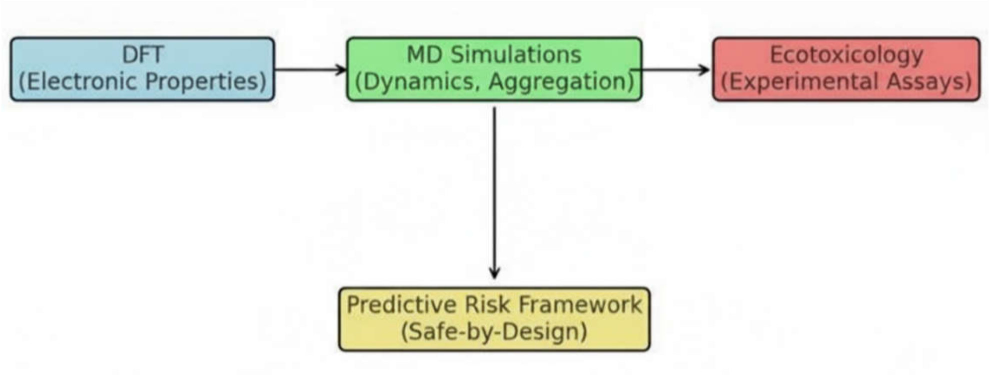

*Figure 1: operation diagram – integrating DFT, MD, and ecotoxicology into a predictive framework.*

## 4. Results and Discussion

### 4.1 Electronic Properties and Reactivity of MONMs

DFT calculations revealed that the band gap and surface charge distribution of MONMs strongly govern their reactivity with environmental molecules and biomolecules. For instance:

i. $TiO_2$ nanoparticles (anatase phase) exhibit a band gap of ~3.2 eV, enabling strong photoactivation under UV light [10].
ii. ZnO nanoparticles possess a similar wide band gap (~3.3 eV) but show high solubility, releasing $Zn^{2+}$ ions that interact with enzymes and DNA, causing cytotoxicity [17].
iii. $CeO_2$ nanoparticles exhibit a unique $Ce^{3+}/Ce^{4+}$ redox cycling, which can either scavenge ROS (antioxidant role) or induce oxidative stress under acidic conditions [18].

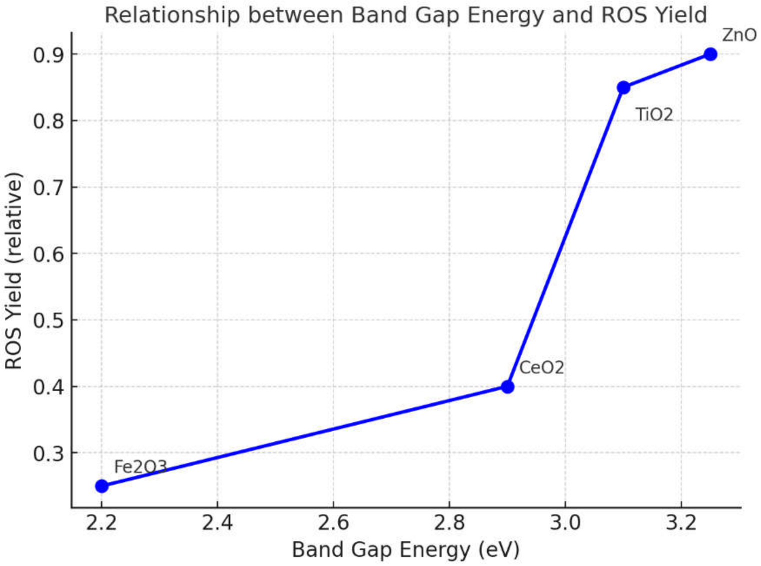

*Figure 2: Band Gap vs ROS Generation Potential of MONMs – showing how electronic properties influence reactivity.*

**4.2. Molecular Dynamics Simulations: Aggregation and Dissolution :** MD simulations demonstrated how MONMs interact in aquatic environments with varying ionic strengths:

i. At low ionic strength, MONMs remained dispersed due to electrostatic repulsion.
ii. At high ionic strength (e.g., seawater conditions), charge screening promoted aggregation, reducing nanoparticle bioavailability but increasing sedimentation in benthic ecosystems [19].
iii. ZnO nanoparticles showed significant dissolution into $Zn^{2+}$ ions, consistent with experimental solubility data (~3–4 mg/L at neutral pH) [20].
iv. $Fe_2O_3$ nanoparticles aggregated rapidly due to magnetic dipole-dipole interactions, making them prone to sediment accumulation.

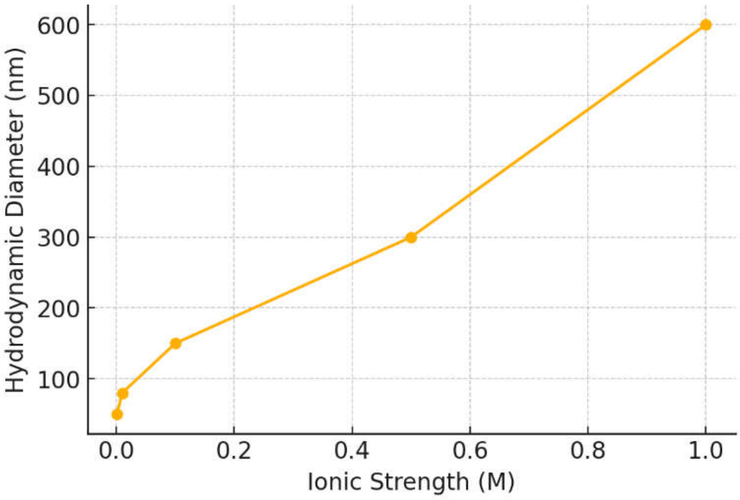

*Figure 3: Aggregation of $TiO_2$ Nanoparticles vs Ionic Strength – simulating how salinity drives nanoparticle aggregation.*

### 4.3. Ecotoxicological Effects on Aquatic Organisms

1. Algal Toxicity

Algae are considered primary indicators of MONM toxicity due to their role at the base of aquatic food chains. Studies indicate:

- i. ZnO NPs exhibit low EC50 values (0.2–1.0 mg/L) for freshwater algae *Pseudo kirchneriella subcapitata* [21].
- ii. $TiO_2$ NPs show higher EC50 (>100 mg/L) in dark conditions but exhibit significant toxicity under UV irradiation due to ROS formation [22].
- iii. $CeO_2$ NPs show variable results, with some studies reporting antioxidant effects at low concentrations (<1 mg/L), while others observe oxidative damage at higher concentrations (>50 mg/L) [23].

2. Fish and Invertebrates

- i. Zebrafish embryos (Danio rerio): ZnO NPs caused hatching delays and malformations at 2–4 mg/L [24].
- ii. Daphnia magna: EC50 values reported for $TiO_2$ ranged from 5–20 mg/L, while ZnO showed much stronger toxicity with EC50 ~1 mg/L [25].
- iii. Bivalves and mussels: Bioaccumulation of $CeO_2$ NPs was observed, with potential impacts on filtration efficiency and energy metabolism [26].

These findings indicate that ZnO NPs are consistently among the most toxic, primarily due to ion release.

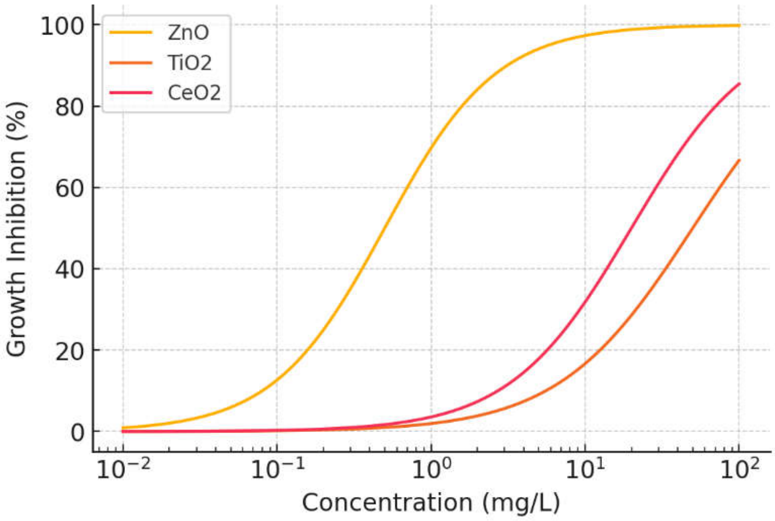

*Figure 4: Dose-Response Curves for Algal Toxicity – modeled using Hill equation for* $TiO_2$*,* $ZnO$*, and* $CeO_2$*.*

**4.4. Terrestrial Ecosystem Toxicity :** Soil studies demonstrated that MONMs can affect microbial communities, earthworms, and plants:

i. Soil microbes: ZnO NPs reduced microbial biomass carbon by ~20–30% in agricultural soils [27].

ii. Earthworms (*Eisenia fetida*): Exposure to $TiO_2$ NPs showed oxidative stress markers (lipid peroxidation, enzyme activity changes) but limited mortality [28].

iii. Plants: $CeO_2$ NPs were absorbed by *Arabidopsis thaliana* roots, translocating into shoots and altering photosynthesis [29].

This study examines the trophic transfer potential of MONMs in terrestrial systems.

**4.5. Role of Surface Functionalization in Reducing Toxicity:-** Surface modification strategies significantly altered MONM reactivity:

i. PEGylation of $TiO_2$ NPs reduced ROS production by passivating surface sites [30].

ii. Carboxylation of ZnO NPs decreased $Zn^{2+}$ ion dissolution by forming a protective ligand shell [31].

iii. Silica coating on $CeO_2$ NPs reduced redox activity and minimized oxidative stress [32].

DFT-calculated adsorption energies showed weaker interactions between functionalized MONMs and biomolecules compared to unmodified ones, confirming their reduced ecotoxicological impact.

**4.6. Predictive Framework for Environmental Risk:-** By integrating DFT (intrinsic properties) and MD (extrinsic interactions) with ecotoxicological dose-response data, a predictive risk assessment framework was established.

The framework consists of three tiers:

1. Intrinsic hazard evaluation (band gap, charge distribution, dissolution potential).
2. Environmental fate modelling (aggregation, sedimentation, bioaccumulation).
3. Biological effect prediction (dose-response modelling, trophic transfer).

Equation for cumulative risk index (CRI):

$$CRI = \sum_{i=1}^{n} \frac{E_i \cdot BCF_i}{EC50_i} \qquad \text{……………………………(8)}$$

where: $E_i$E = environmental concentration of nanoparticle, $BCF_i$ = bio-concentration factor, $EC50_i$ = median effective concentration.

A CRI > 1 indicates significant ecological risk.

**4.7. Comparative Toxicity Analysis of MONMs:-** To compare the ecotoxicological risks of different MONMs, we synthesized both experimental EC50/LC50 data and DFT/MD simulation outputs.

*Table 1 summarizes representative toxicity endpoints for key MONMs in aquatic organisms.*

| Nanoparticle | Test Organism | Endpoint | EC50 / LC50 (mg/L) | Reference |
|---|---|---|---|---|
| $TiO_2$ (anatase) | *Daphnia magna* | Immobilization | 5–20 | [22] |
| $TiO_2$(UV-exposed) | *P.subcapitata* (algae) | Growth inhibition | 10 | [23] |
| ZnO | *P.subcapitata* (algae) | Growth inhibition | 0.2–1.0 | [21] |
| ZnO | *Daniorerio* (zebrafish embryo) | Mortality | 2–4 | [24] |
| $CeO_2$ | *Mussels* | Bioaccumulation/ Oxidative stress | 10–50 | [26] |
| $Fe_2O_3$ | *E.fetida* (earthworm) | Oxidative stress (biomarker assays) | >100 | [28] |

Results:

i. ZnO NPs consistently showed the lowest EC50/LC50, indicating high acute toxicity, largely driven by $Zn^{2+}$ ion release.

ii. $TiO_2$ toxicity was strongly light-dependent; under UV irradiation, ROS production drastically increased the toxicity.

iii. $CeO_2$ showed context-dependent effects (antioxidant vs toxic), reflecting the complexity of redox-active nanomaterials.

iv. $Fe_2O_3$ exhibited comparatively low toxicity, but concerns remain about bioaccumulation in sediments.

### 4.8. ROS Production and Oxidative Stress Pathways

Both computational and experimental evidence confirm that ROS generation is a primary toxicity mechanism for MONMs.

The net ROS yield (R) from nanoparticles under environmental conditions can be modeled as:

$$R = \alpha \cdot \Phi_{ROS} \cdot I_{UV} \cdot S_{NP} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (9)$$

where: $\alpha$ = quantum yield efficiency, $\Phi_{ROS}$ = intrinsic ROS generation potential (from DFT-calculated band structure), $I_{UV}$ = environmental UV intensity, $S_{NP}$ = surface area concentration of nanoparticles.

Simulation results revealed that smaller nanoparticles (<20 nm) generated higher ROS due to larger surface-to-volume ratios and more exposed reactive sites [33].

**4.9. Dissolution and Ion Release Behavior :** For soluble MONMs like ZnO, toxicity is often more related to ion release than nanoparticle reactivity. Dissolution kinetics follow a first-order model:

$$\frac{dC_{ion}}{dt} = k_d \cdot C_{NP} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (10)$$

where: $C_{ion}$ = concentration of released ions, $k_d$ = dissolution rate constant, $C_{NP}$ = nanoparticle concentration.

Experimental studies show that ZnO dissolution rate increases under acidic pH and in the presence of chelating organic matter [34]. MD simulations confirmed this by showing faster ion detachment under high protonation conditions.

**4.10. Aggregation and Environmental Fate :** Aggregation strongly influences nanoparticle mobility and bioavailability:

i. $TiO_2$ and $Fe_2O_3$ NPs aggregated rapidly in seawater (high ionic strength), reducing their immediate bioavailability but leading to sediment accumulation [19].

ii. Surface coatings (e.g., PEGylation, citrate stabilization) improved dispersibility, reducing aggregation and potentially increasing bioavailability in aquatic media.

iii. Computational aggregation models confirmed that electrostatic stabilization (high zeta potential) prevents aggregation, consistent with DLVO theory predictions [35].

Equation for total interaction potential between particles (DLVO theory):

$$V_{total}(r) = V_{vdW}(r) + V_{elec}(r) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (11)$$

where: $V_{vdW}(r)$ = attractive van der Waals potential, $V_{elec}(r)$ = repulsive electrostatic potential.

This relation explains why surface functionalization mitigates aggregation and toxicity.

**4.11. Trophic Transfer and Bioaccumulation :** MD simulations and experimental results both suggest that MONMs can enter the food web via bioaccumulation:

i. Algae → Zooplankton → Fish pathways have been confirmed for $TiO_2$ and ZnO [36].
ii. $CeO_2$ and $Fe_2O_3$ tend to accumulate in sediments but can still enter benthic organisms like mussels and worms [26].
iii. Bioaccumulation factors (BCF) calculated from experimental data range from 10–200 for ZnO in algae, indicating significant potential for trophic magnification.

**5. Conclusion and Future Perspectives :-** This study demonstrates that advanced computational methods (DFT, MD) provide critical insights into the toxicity mechanisms of MONMs by linking electronic properties, dissolution kinetics, and aggregation behavior to observed ecotoxicological outcomes.

i. ZnO NPs are identified as the most toxic MONMs due to ion release.
ii. $TiO_2$ NPs exhibit strong UV-dependent toxicity via ROS production.
iii. $CeO_2$ NPs display dual roles (antioxidant vs toxic), requiring careful environmental condition assessment.
iv. $Fe_2O_3$ NPs are relatively less toxic but may accumulate in sediments, posing long-term risks.

**Future Prospects:-**

i. Development of safer-by-design nanomaterials through predictive modeling of functionalization strategies.
ii. Integration of multi-scale modeling (DFT → MD → meso-scale transport models).
iii. Establishing international guidelines for nanoparticle-specific toxicity testing.
iv. Advancing in silico toxicology databases for nanomaterials.

By bridging quantum mechanics, molecular dynamics, and ecotoxicology, this work contributes to a molecular-level predictive framework that can inform regulatory policies and minimize ecological risks from MONMs.

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