# Nanotoxicity: are our allayed fears about toxicity of nanomaterials correct?

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#### Nanomaterials







Graphene oxide Carbon quatum dots Graphene quantum dots Fullerene



The same properties that make nanomaterials interesting can also make them harmful

- Enhanced reactivity
- Increased surface to mass ration
- Enhanced permeation
- Relevant quantum effects
- Previously unknown forms of materials

#### Toxicity of nanomaterials



Toxicity tests may be performed employing live (in vivo) organisms, such as microcrustaceans, fishes, rodents, and other animals and/or cell cultures (in vitro).

Several standardized toxicological tests are available to measure the biological response of an organism to a chemical. However, there is no standardization for the evaluation of the toxicity of nanomaterials, which hampers the comparison of results and the consensus about their toxicity. Most of the studies performed so far are adaptations of the standard procedures used for other substances

# Toxicological assessment of nanoparticles

The toxicity of nanoparticles depends on their sizes, material concentration, charge, material composition and their stability. The in vitro and in vivo toxicological assessment are carried out with emphasis on the histological changes, biodistribution, pharmacokinetic influence, biochemistry metabolism, and clearance.

Nanotoxicity tests of ZnO synthesized using hibiscus leaf extract



Periwinkles were exposed for 10 days at different concentrations of ZnO NPs and at the termination of the experiment, no mortality was recorded





Healthy periwinkles before and after exposure

Nanomaterial	Mean diameter of the particles (nm)	Test organism	Main results
Ag	13–17 nm	<i>Lymnaea stagnalis</i> (Mollusca)	Growth alteration and bioaccumulation
ZnO TiO <sub>2</sub>	15–30 nm	Skeletonema marinoi (Diatom— Skeletomataceae), Thalassiosira pseudonana (Diatom— Thalassiosiraceae), Dunaliella tertiolecta (Algae— Dunaliellaceae), Isochrysis galbana (Algae— Isochrysidaceae)	Only nanoparticles of ZnO have decreased growth rate of diatom and algae population
Graphene family nanoparticles	8 <u>—</u> 8	Caenorhabditis elegans (Nematoda)	Decreased reproduction rates

ZnO CuO AgO	ZnO: 20–30 nm CuO: 20–100 nm AgO: 20–70 nm	Thalassiosira weissflogii (Diatom— Thalassiosiraceae)	Decreased diatom population growth in similar way to respective dissolved metals. Bioaccumulation of nanoparticles in cell wall and possible transfer through trophic chain		
ZnO Al <sub>2</sub> O <sub>3</sub> TiO <sub>2</sub>	10	Danio rerio (Chordata)	Metal oxide nanoparticles induced different toxic effects in zebrafish development according to each metal. ZnO delayed larvae and embryo development and also induced serious ulceration in larvae		
TiO <sub>2</sub>	~43 nm	Pimephales promelas (Chordata)	Fish immunotoxicity and gene expression alteration		
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TiO <sub>2</sub>	5, 10, and 32 nm	Xenopus laevis (Chordata)	Significantly affected tadpole growth. The highest concentration caused mortality, suppressed tadpole body length, and delayed animal development		

TiO2	le(	Daphnia similis (Crustacea)	The highest concentration (100 mg L <sup>-1</sup> ) did not induce toxic effects under experimental conditions. A mixture of TiO <sub>2</sub> forms induced toxic effects by ROS generation when exposed to UVA light
TiO <sub>2</sub>	TiO <sub>2</sub> :	Vibrio fischeri	Suspensions of
ZnO	25–70 nm	(Gammaproteobacteria),	nano- and bulk
CuO	ZnO:	Daphnia magna	TiO <sub>2</sub> were not
	50–70 nm	(Crustacea),	toxic. A nano-ZnO
	CuO: 30 nm	Thamnocephalus platvurus (Crustacea)	formulation was verv toxic to V
		1	fischeri, D. magna, and T. platyurus.
			Cu compound
			also showed
			toxicity; however,
			for Daphnia
			magna were less
			bioavailable than
			for bacteria

Metallic nanoparticles of Ag, Cu, Al, Co, Ni and TiO <sub>2</sub>	Ag (20– 30 nm), Cu (15– 45 nm), Al (51 nm), Co (10– 20 nm), Ni (5–20 nm), and TiO <sub>2</sub> (30 nm)	Raphidocelis subcapitata (Algae— Selenastraceae), Ceriodaphnia dubia (Crustacea), Daphnia pulex (Crustacea), Danio rerio (Chordata)	Nanometals caused acute toxicity in multiple aquatic organisms, but the effect was different according to the metal particle and the species used. Since <i>R.</i> <i>subcapitata</i> , <i>C.</i> <i>dubia</i> , and <i>D. pulex</i> were susceptible to nanometals, trophic chain could be compromised
 Ag ZnO	Ag (15 nm) ZnO	Raphidocelis subcapitata (Algae—	Ag and Cu nanoparticles
CeOr	(34-42 nm)	Danhuia magua	arrected all
Cu	(10-23  nm)	(Crustacea) Danio verio	was toxic to algae
	CeO <sub>2</sub>	(Chordata)	and daphnids; TiO <sub>2</sub>

# Phytotoxicity evaluation of green synthesized nanoparticles on flax seeds

As regards silver nanoparticles, at first, they stimulated the growth of garden cress. Next, the growth was hindered, and later it was stimulated once again. The solution of silver nanoparticles stimulated fax growth at all tested concentrations. Those results demonstrate that silver nanoparticles synthesized biologically using V. officinalis extract are nontoxic. They also suggest that fax germination is somehow resistant to the negative impact of silver nanoparticles. Flax germination was shown to undergo no signifcant changes due to any type of treatment, regardless of concentrations (El-Temsah and Joner, 2012).



	and		
(A)	( <b>B</b> )	(C)	(D)
	Veronica officinalis extract	Solution of AgNO <sub>3</sub>	Biosynthesized silver nanopar- ticles
IC <sub>50</sub> for L. flavum (mga ml)	3.3927	0.0171	nt
IC <sub>50</sub> for L. sativum (mg ml)	g/ nt	0.0125	nt

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### Toxicity Assessment of Cellulose-Ag-ZnO Nanocomposites Using Onions Bulb Plant



	Mean Length (cm)					Mean SD	SD	SE	SGR	Mean length	% Growth
	1	2	3	4	5					5 <b>H</b>	8 0 k
Conc., m	g/L							1.01	10.110	100	
0	6.00	5.50	6.50	5.30	5.00	5.66	0.50	0.29	0.059	5.66	100
3.125	5.70	5.90	5.40	4.60	5.30	5.38	0.25	0.15	0.056	5.38	95
6.25	4.10	4.30	4.00	4.00	3.70	4.02	0.15	0.09	0.042	4.02	71
12.5	3.80	3.90	4.00	3.50	2.90	3.62	0.10	0.06	0.038	3.62	64
25	3.10	2.50	2.30	2.80	2.00	2.54	0.42	0.24	0.027	2.54	45
50	2.00	2.50	2.80	2.20	2.10	2.32	0.40	0.23	0.024	2.32	41

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## Cytotoxicity of Ag, Au and Ag-Au bimetallic nanoparticles prepared using golden rod (Solidago canadensis) plant extract

Behaviour of NPs in biological media or determination of their toxic potency depend on material constitution or arrangement. Shapes of nanoparticles are important in determining toxicity. For instance, triangular-shaped silver nanomaterials exhibit greater toxic potency relative to spherical NP. Surface area, large ratio of surface atoms to bulk atoms results in greater reactivity and toxic potencies



Comparison of pre normalized CI values between H4IIEluc cells (cyan) and HuTu-80 cells (blue) control cells and blank wells containing only NPs indicating no particle interference.



Growth curves of HuTu-80 cells exposed to three concentrations of Au-NPs for 100h (Blue: Control; Purple: 5  $\mu$ g/mL; Pink: 25 $\mu$ g/mL; Red: 50  $\mu$ g/mL). Te line indicates addition of the nanomaterials as well as normalization time point



Growth curves of HuTu-80 cells exposed to Ag-NPs for 100h (Blue: Control; Purple: 5 μg/mL; Yellow: 25μg/mL; Black: 50μg/mL).



Growth of H4IIE-luc cells s in the presence of three concentrations of Au-NPs for 100h (Cyan: Control; Purple: 5 µg/mL; Pink: 25µg/mL; Red: 50µg/mL).



Growth curves of HuTu-80 cells exposed to Ag-Au-BMPs for 100h (Blue: Control; Orange: 5  $\mu$ g/mL; Dark green: 25  $\mu$ g/mL Green: 50  $\mu$ g/mL).



. Growth curves of H4IIE-luc cells exposed to three concentrations of Ag-NPs for 100h (Cyan: Control; Purple: 5 μg/mL; Yellow: 25 μg/mL; Black: 50μg/mL).



BNPs exhibited the greatest toxic potency to these two types of cells

Growth curves of H4IIE-luc cells exposed to three concentrations of Ag-Au-BMPs for 100h (Cyan: Control; Orange: 5 μg/mL; Dark green: 25 μg/mL; Green: 50 μg/mL).

H4IIE-luc cells exhibited statistically significant diferences in cells exposed to the two greatest concentrations (25 and 50µg/mL) of all three types of NPs. Au-NPs significantly stimulated growth of cells while both Ag-NPs and Ag-Au-BMPs caused significant decreases in viability of cells. The least concentration (5 µg/mL) of Ag-NPs and Au-NPs caused non-significant stimulation of growth of cells, while Ag-Au-BMPs caused a significant decrease in cell viability of H4IIE-luc cells

# Conclusion

Contact with materials in the nanoscale may result in penetration of various kinds of cells, which is a very important potential consequence. Nanoparticles exercise a direct impact on algae, plants and fungi by entering into redox reactions with organic particles, which disturbs the processes of photosynthesis and respiration. Cellulose cell walls of algae and higher plants, as well as chitin walls of fungi, have small pores with the diameter of 5–20 nm, and nanoparticles may induce creation of larger pores. After penetrating cell wall, nanoparticles encounter the cytoplasmic membrane. The membrane becomes convex, encloses nanoparticles in bubbles and pulls them in the cell. The majority of the reported phytotoxicity studies used nanoparticles synthesized by means of chemical methods.



Not all biologically synthesized nanomaterials are necessarily safe.

Example: AuNPs synthesized from golden rod extract exhibited lesser toxic potency than NPs synthesized without plant leaf extracts.



The Head of Lautech Nanogroup

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