

Nanotechnology: From Harmful to Helpful?

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The Two Faces of Nanotechnology

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BY MARK HENDERSON, SCIENCE CO

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In Study, Researchers Find Nanotubes May Pose Health Risks Similar to Asbestos

By KENNETH CHANG
Published: May 21, 2008

Nanotubes, one of the wonder materials of the new age of nanotechnology, may carry a health risk similar to that of asbestos, a wonder material of an earlier age that turned into a scourge after decades of use when its fibers were found to cause [lung disease](#), researchers said Tuesday.

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Another Risk vs. Benefit Tension

.... Hormesis

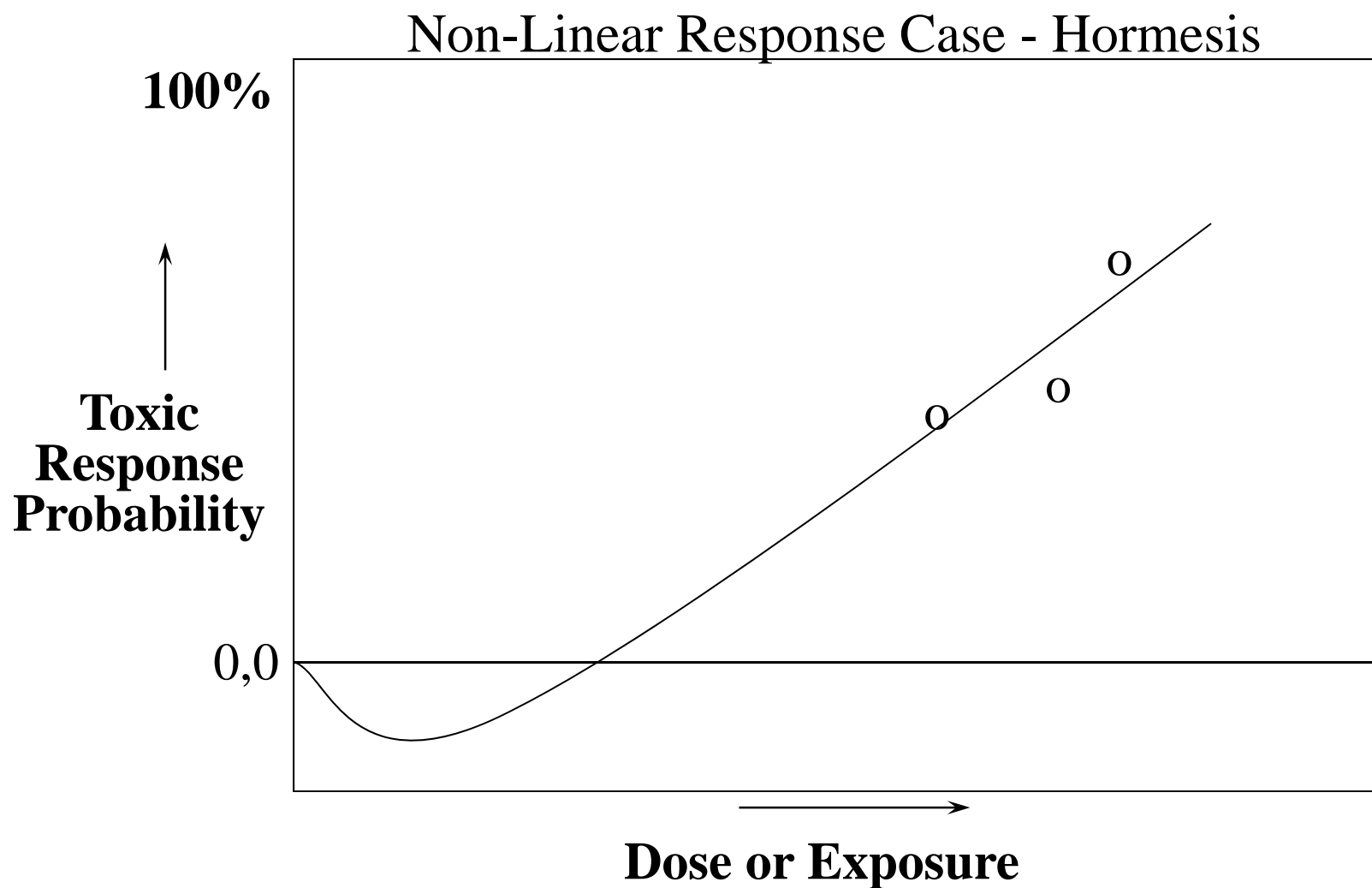
Hormesis

Definition:

- Dose response phenomenon characterized by a low dose stimulation and a high dose inhibition.
- Generally similar quantitative features with respect to amplitude and range of the stimulatory response.
- May be directly induced or the result of compensatory biological processes following an initial disruption in homeostasis.

Source: Edward Calabrese

Dose-Response Curve



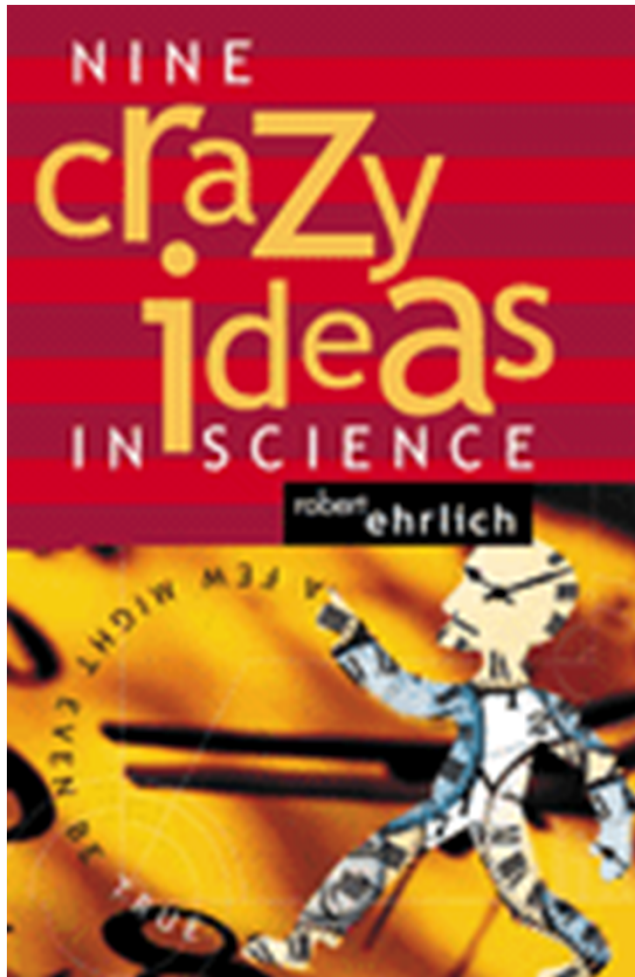
nature

February 13, 2003

Dangerous levels of toxins
miscalculated

Potential pollutants and poisons may be
beneficial in low doses.

Hormesis: Public Perception



- “Man [or woman] in the street” has incredulous response to hormesis
- Media would likely have a field day skewering adoption of hormesis

Evidence of Hormesis

General Summary:

- Hormesis databases: thousands of dose responses indicative of hormesis
- Hormesis is a very general phenomenon: independent of model, endpoint and agent
- Frequency of hormesis: far more frequent than threshold model in fair head-to-head comparisons

Source: Edward Calabrese

Hormesis and Nanotechnology

1. Do nanomaterials exhibit a hormetic dose response relationship?
2. If hormesis applies to nanomaterials, what is significance for risk assessment and risk management?

1. Do nanomaterials exhibit a hormetic dose response relationship?

The Scientific Basis for the Regulation
of Nanoparticles: Challenging
Paracelsus and Paré

UCLA J. Envtl L. (201)

*Bernard D. Goldstein, MD**

- Some critics of hormesis (e.g., Lisa Heinzerling) have argued that hormesis may be relevant for physical or chemical agents that humans have evolved with, but not synthetic chemicals
- Since we have always been exposed to natural nanoparticles, “it could be argued, since humans have evolved in the presence of nanoparticles, we should have little to worry about.”

Table 1: Ultrafine/Nano Particles (<100 nm): Natural and anthropogenic sources.

Natural	Anthropogenic		
	Unintentional	Intentional	
Gas to particle conversions	Internal combustion engines	Engineered nanoparticles:	
Forest fires	Power plants	(<i>controlled size and shape,</i>	
Volcanoes (hot lava)	Incinerators	<i>designed for functionality)</i>	
Viruses	Airplane jets	<i>metals, semiconductors, metal oxides</i>	
Biogenic magnetite:	Metal fumes	<i>carbon, polymers</i>	
<i>magnetotactic bacteria</i>	<i>(smelting, welding, etc.)</i>	<i>nano-spheres, -wires,</i>	
<i>protocists, mollusks,</i>	Polymer fumes	<i>-needles, -tubes, -shells,</i>	
<i>arthropods, fish, birds</i>	Other fumes	<i>-rings, -platelets;</i>	
<i>human brain, meteorite?</i>	Heated surfaces	<i>untreated, coated</i>	
Ferritin (12.5 nm)	Frying, broiling, grilling	<i>(nanotechnology applied to many</i>	
Microparticles (<100 nm)	Electric motors	<i>products: cosmetics, medical, fabrics,</i>	
<i>(activated cells)</i>		<i>electronics, optics, displays, etc.)</i>	
<u>Portals of Entry</u>			
<i>Respiratory Tract</i>	<i>GI-tract</i>	<i>Skin</i>	<i>Injection</i>
<i>Inhalation</i>	<i>Ingestion</i>	<i>Dermal</i>	<i>Blood Circulation</i>

Exposure: Natural vs. Incidental vs. Engineered Nanoparticles

- Average person consumes approx. 10 trillion submicron-sized particles per day in normal diet
- Outdoor concentrations of incidental nanoparticles in cities range from 5000 to 3 million particles/cm³
 - corresponds to breathing in 54 billion-324 trillion nanoparticles per day

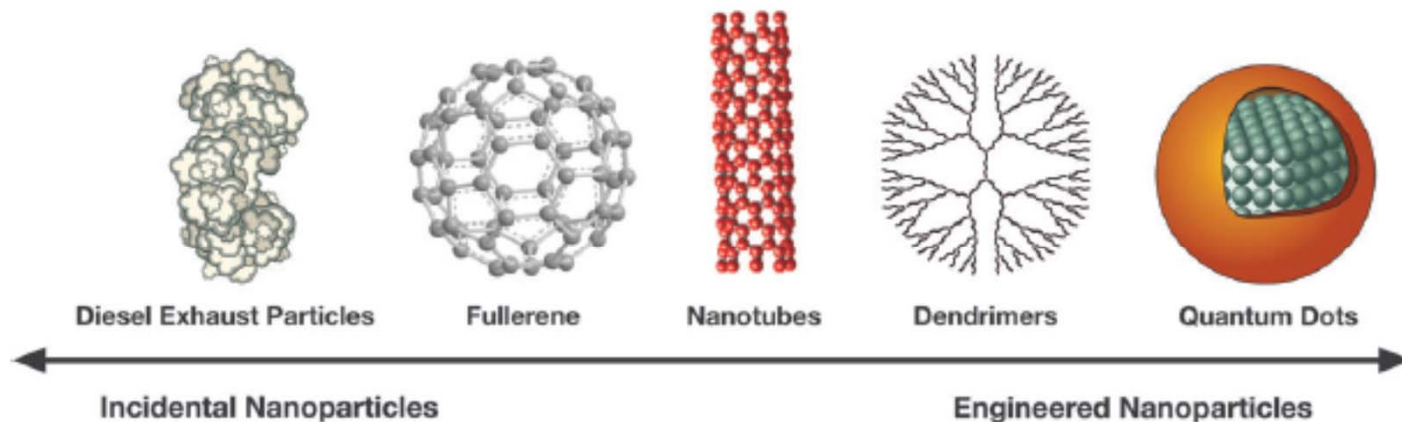


FIG. 1. Examples of incidental and engineered nanoparticles.



Contents lists available at [ScienceDirect](#)

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Review

Hormetic dose–responses in nanotechnology studies

Ivo Iavicoli ^{a,1}, Luca Fontana ^{a,1}, Veruscka Leso ^{a,1}, Edward J. Calabrese ^{b,*}

^a *Institute of Public Health, Università Cattolica del Sacro Cuore, Largo Francesco Vito 1, 00168 Roma, Italy*

^b *Environmental Health Sciences, School of Public Health & Health Sciences, University of Massachusetts, Morrill I, N344, Amherst, MA 01003, USA*

HIGHLIGHTS

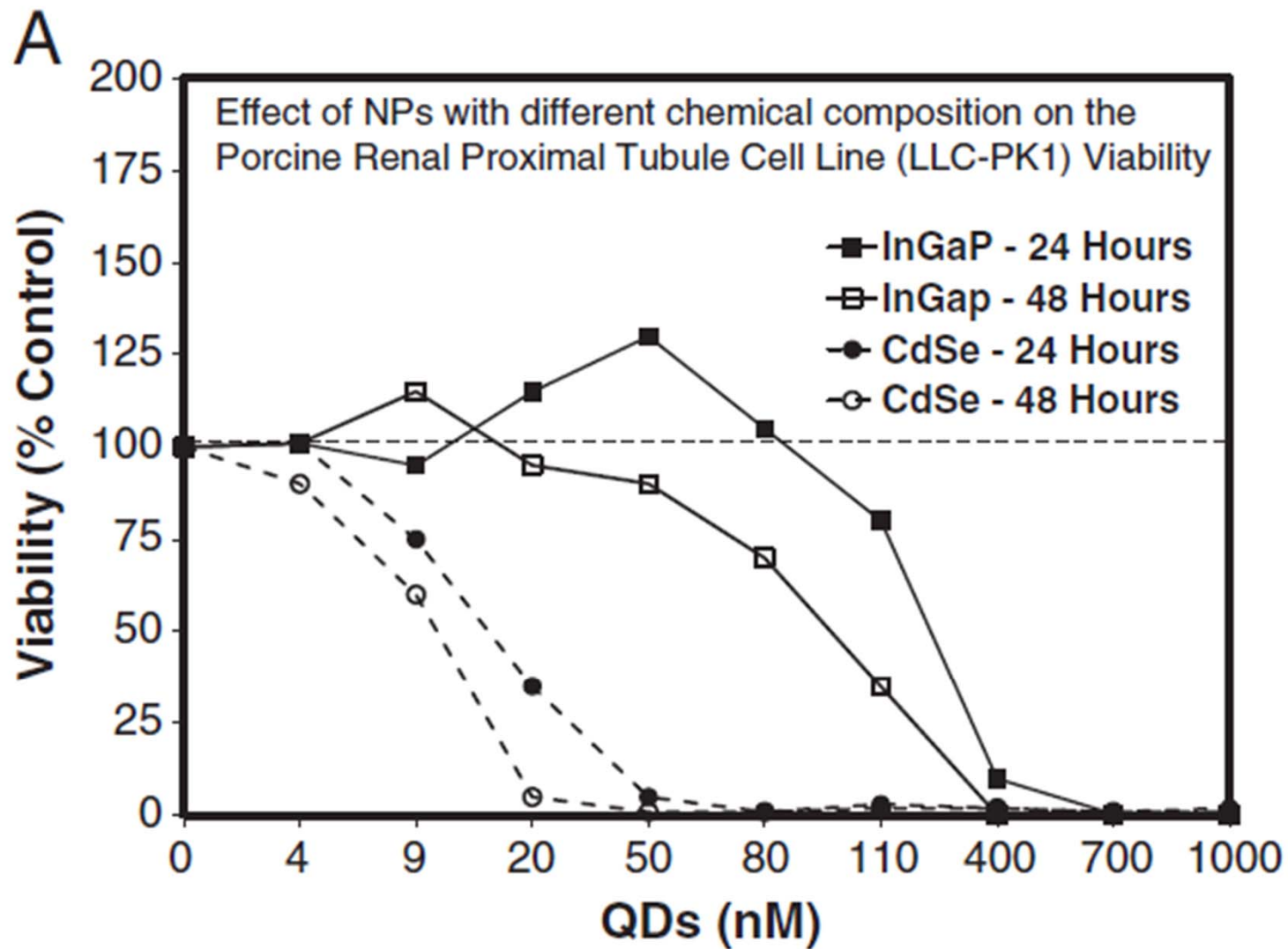
- Nanoparticles induce hormetic-like biphasic dose-responses in biological models.
- Nanoparticle-induced hormetic response can depend on physico-chemical properties.
- The maximum stimulatory responses of the hormetic curves were generally modest.
- Hormesis induced by NPs is quantitatively similar to the induced by other agents.

Iavicoli et al (2014):

Conclusion

- “Different types of NPs such as CNTs, QDs, metal and metal oxide NPs and NRDE-NPs induce a hormetic response both in in vitro and in vivo models. The maximum stimulatory responses of the hormetic curves were generally modest, usually not exceeding the ~30 to 60% increase over the control value.”

Effect of Chemical Composition



Iavicoli et al (2014):

Hormesis and Nanotechnology: Study Design Issues

- “In general, the studies in which such hormetic-like biphasic dose responses were reported were not prospectively designed to test for possible hormetic effects. Only several reviewed articles explicitly refer to the hormetic dose response model when interpreting their results. Furthermore, in several studies the biphasic dose response phenomenon is not mentioned or discussed, despite results suggesting this hypothesis. Therefore, the hormetic concept may be underestimated. In this context, future studies evaluating the potential NP toxic effects should consider the possibility of hormetic responses in study design, biological model and endpoint selection, and statistical analysis.”

Iavicoli et al (2014)

2. If hormesis applies to nanomaterials, what is significance for risk assessment and risk management?

Handling nanotube material



Raw single walled nanotube material

Reasons for Agency Reluctance to Consider Hormesis

- Uncertainties about dose, susceptible groups, mechanism, etc.
- Contrary to traditional mission of reducing toxic exposures as low as possible
- Additional demand on limited resources
- Further complication of risk assessment
- Politically volatile
- Potential for media sensationalization
 - (cf Nine Crazy Ideas in Science, R. Ehrlich (2001))

Data Limitations That May Limit Utilization of Hormesis

- Uncertainties about exposure levels at which hormesis occurs and magnitude of protective effect
- Cumulative exposures (same/other agents)
- Susceptible sub-groups
- Different endpoints
- But should these problems have greater force for hormesis than other low-dose models?

- Emphasis on post-market surveillance rather than pre-market approval (Goldstein)