Book Review: Particle Toxicology

Ken Donaldson & Paul Borm, Eds; 2007;
CRC Press: Boca Raton. ISBN-10: 0-8493-5092-1

Dr Steven M Hankin, Consultant Chemical Toxicologist at the Institute of Occupational Medicine reviews 'Particle Toxicology'.

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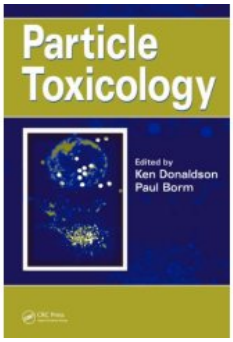

Book Review: *Particle Toxicology*

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Exposure to particles in industry and the environment constitutes an ongoing, but dynamic, potential risk to health in many sectors and locations. When reading *Particle Toxicology*, the general theme that extends from the introductory chapter into the remainder of the book is one of developments of particle research, from a historical perspective, from coal mining, fibre-related disease, ambient particulate matter, to potentially new risks presented by engineered nanomaterials.

Particle Toxicology shows how modern toxicology considers particle size, exposure concentrations, target populations, and endpoints that lead to local and systemic effects including adverse cardiovascular and neurological outcomes. The book's 22 chapters generally fall into one of three overlapping themes: *mechanistic studies*; *endpoints & effects*; and *characterisation, testing and modelling.* Contributions from leading researchers address topics including particle-associated pro-inflammatory effects and inflammatory signalling, cellular and extra-cellular oxidative and nitrosative stress, particulate interactions in the pulmonary, cardiovascular, and central nervous systems, toxicological testing and modelling, as well as susceptibility and genotoxic effects. The particle types considered include silicates, asbestos, metals, anthropogenic particulate matter and nanoparticles. Chapters that give particular emphasis to nanomaterials, include those on the interaction of particles with membranes, the use of nanomaterials in medicine, and specific sections on extending exposure-dose-response models to the translocation of nanoparticles.
Having set the context in the opening chapter, the editors propose four critical issues for consideration when developing the research and regulation agenda: i) the importance of possible read-across of effects observed in different engineered nanoparticles; ii) new effects in new exposure scenarios; iii) the absence of ecotoxicity and absorption, distribution, metabolism & excretion (ADME) studies; and iv) that testing should be driven by materials' applications. Some aspects of these four issues are considered in the book's subsequent chapters; others remain for future consideration.

After a concise description of the physico-chemical characteristics of pathogenic particles and the principles of particle dosimetry (including deposition, retention & clearance, and translocation) a series of chapters focus on the current mechanistic evidence behind particle-mediated oxidative stress, inflammation in the lung, and interstitial pulmonary fibrosis. Complementing the mechanistic theme is a short chapter that highlights the potential contribution of particle-associated organics to pro-inflammatory signalling. Particles, particularly those carbonaceous in nature derived from combustion processes, are often accompanied by a complex range of organic compounds, including polycyclic aromatic hydrocarbons (PAHs), nitroaromatic hydrocarbons, aldehydes and heterocyclics. Although generally not present in concentrations that invoke toxic responses themselves, it is clear that these organic compounds play an important role in the adverse effects of atmospheric particles.

Evidence that the effects of inhaled particles are no longer confined to the lung, with nanoparticles possessing the potential to translocate to the bloodstream, the brain, and other target sites is presented. The current, limited, knowledge of the effects and mechanisms of action of particles on the immune system is described briefly followed by the more developed evidence-base of effects on the cardiovascular system. Ongoing research in both areas is advocated and, where active already, anticipated to reveal not only

which mechanistic pathways are most relevant to the associated epidemiology but to give valuable insight into assessing the risks of disease from exposure and the possibility of therapeutic interventions to reduce the impact of environmental particulate matter on cardiovascular disease. This is followed by a discussion of genetic and non-genetic factors that have been found to contribute to inter-individual susceptibility and which provides a perspective on the relative importance of these factors, primarily as a lead to further research.

Approaches to the *in vitro* and animal-based testing of particle toxicology are discussed, concluding with a recommendation of a tiered approach for testing particles of unknown toxicity that offers the prospect of tailoring a testing regime that can identify early a material's toxic responses prior to animal testing, and that may also identify key aspects of toxicity to investigate in more specialised protocols.

Mathematical modelling of exposure, dose and response (dosimetric modelling) to substances is an important specialism in toxicology, whose aim is to establish a robust means of assessing the effects of substances on health and the environment that at the very least compliments and informs (and may ultimately reduce or replace) the need for experimental testing of substances of unknown hazard. The key feature of modelling is the extrapolation of exposure, dose and response data between substances and between species. As with all mathematical modelling, dosimetric modelling makes the most plausible contribution to toxicology when based on a good understanding of the underlying mechanisms. Two novel and compatible biomathematical models (rat and human based) are described that facilitate biologically-based extrapolation from the rat to human for parameters not available for humans.

Particle Toxicology considers one 'application' of particles and the relevant exposure and toxicology: nanomaterials in medicine. The chapter provides a good overview of the use of nanoparticles in cellular and tissue imaging, diagnostic tools, medical implants and drug delivery vehicles. Hazards and risks of nanoparticles from these applications and others being considered (e.g. microbicides) are discussed broadly and the chapter concludes with recommendations for a multidisciplinary approach that considers the impact of direct and concomitant effects from both the 'active' and 'carrier' components of intentionally and unintentionally released nanoparticles in medical applications.

The book's concluding chapter seeks to draw together the threads from the preceding chapters and present a new unifying concept taking the discipline forward into the area of nanotoxicology and highlighting the following two key questions: i) *what* is it about particles that make them harmful or not? and ii) *how* do harmful particles cause harm? Consideration, albeit underdeveloped as acknowledged by the authors, is given to a new concept, paradigm, or framework for particle toxicology when considering nanomaterials.

In summary, *Particle Toxicology* provides a review of the current knowledge and new concepts towards understanding mechanistic actions, effects, and toxicological characterisation of pathogenic particles. *Particle Toxicology* has been published in timely response to the developing interest both in consumer applications of nanomaterials and research to develop the field of particle risk assessment.

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