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A new paradigm in application of interspecies physiologic and allometric scaling and its human relevance in toxicological risk evaluation

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During the past few years, there has been a paradigm shift in the field of toxicological risk assessment for chemicals, including an emerging consensus on the need for a flexible, innovative and interdisciplinary science-based approach for investigative toxicology. As a matter of necessity, the potential for a chemical agent to produce adverse health effects in humans is investigated in experimental animals, typically rodents and non-rodents. Toxicological effects observed in the experimental animals may be taken as evidence that humans might show similar responses to equivalent chemical exposures. The use of these surrogates is premised upon the high degree of unique physiological, biochemical and anatomical similarities or variations among mammalian species. This uniqueness is reflected by inter-species differences in protein binding, drug metabolism and drug transport in pharmacokinetic phase and changes in receptor expression, affinity and distribution in pharmacodynamic phase to result in interspecies variation in toxicity profile. Allometric scaling is an empirical approach which considers these species differences including body surface area in normalization of different parameters. Interspecies scaling is not without short comings and failures. Over the years, interspecies scaling has drawn enormous attention and new scaling methods have been developed in order to improve the performance of these predictions. During dose-response extrapolation and setting acceptable levels of human exposure, a quantitative relationship between the dose levels in humans and in animals is to be specified, that is expected to result in the same degree of adverse effect. The empirical data on comparative toxicological potencies support the general practice of scaling animal potencies to humans and theoretical support for scaling toxicity should be available from analysis of the allometric variation of key physiological parameters across mammalian species. Such an analysis has the benefit of providing an articulated rationale for the scaling methodology and of setting out the underlying assumptions explicitly.

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Ameliorating effects of Thymoquinone on Titanium Dioxide nanoparticles induced toxicity in rats

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The ameliorating effect of Thymoquinone (TQ), the major active ingredient of *Nigella sativa* seeds, on Titanium Dioxide naonparticles (TiO_2 NPs) induced toxicity and oxidative stress in Sprague-Dawley (SD) rats was investigated. 40 rats were divided into 4 equal groups. The first, second, third and fourth groups received TiO_2 NPs, TiO_2 NPs and TQ, TQ only for 6 weeks. The fourth group served as the control. Exposure to TiO_2 NPs resulted in increased liver enzyme markers, oxidative stress indices, tumor necrosis factor alpha (TNF-α) and DNA damage was assessed by comet assay. TiO_2 NPs resulted in decreased level of testosterone hormone. Histopathological alterations were also observed in the liver, brain, lung and testes. Transmission electron microscopy revealed changes in the hepatocytes cytoplasm related to the oxidative stress and presence of nanoparticles in the testicular tissues. Co-administration of TQ with TiO_2 NPs decreased the level of liver enzymes, oxidative stress, TNF-α and DNA damage and ameliorates the level of testosterone. Furthermore, TQ increased the total antioxidant and glutathione (GSH) levels. In conclusion, TiO_2 NPs induce hazardous effects in different organs and are closely related to oxidative stress. TQ have anti-oxidative and anti-inflammatory effect against the detrimental effect of TiO_2 NPs.

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