

## Safety assessments of subcutaneous doses of aragonite calcium carbonate nanocrystals in rats

### ABSTRACT

Calcium carbonate nanoparticles have shown promising potentials in the delivery of drugs and metabolites. There is however, a paucity of information on the safety of their intentional or accidental over exposures to biological systems and general health safety. To this end, this study aims at documenting information on the safety of subcutaneous doses of biogenic nanocrystals of aragonite polymorph of calcium carbonate derived from cockle shells (ANC) in Sprague-Dawley (SD) rats. ANC was synthesized using the top-down method, characterized using the transmission electron microscopy and field emission scanning electron microscope and its acute and repeated dose 28-day trial toxicities were evaluated in SD rats. The results showed that the homogenous  $30 \pm 5$  nm-sized spherical pure aragonite nanocrystals were not associated with mortality in the rats. Severe clinical signs and gross and histopathological lesions, indicating organ toxicities, were recorded in the acute toxicity (29,500 mg/m<sup>2</sup>) group and the high dose (5900 mg/m<sup>2</sup>) group of the repeated dose 28-day trial. However, the medium- (590 mg/m<sup>2</sup> body weight) and low (59 mg/m<sup>2</sup>)-dose groups showed moderate to mild lesions. The relatively mild lesions observed in the low toxicity dosage group marked the safety margin of ANC in SD rats. It was concluded from this study that the toxicity of CaCO<sub>3</sub> was dependent on the particulate size ( $30 \pm 5$  nm) and concentration and the route of administration used.

**Keyword:** CaCO<sub>3</sub>; Invivo; Nanotoxicity; Cockleshell; Aragonite