Title : A physiologically base pharmacokinetic (PBPK) model for risk assessment of melamine exposed children with nephrolithiasis in Taiwan

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Melamine, an artificial raw material, is commonly used in industrial products such as food containers, housewares, furniture, fabrics, fire retardant paint and more. Due to the characteristic of melamine is high nitrogen content, it becomes an illegitimate additive in dietary to increase the non-protein nitrogen. Melamine has low acute toxicity but overdose exposure in animals can cause nephrolithiasis. In 2007, the wheat gluten contained melamine was involved in cases of acute renal failure in pets (1). Because of a recent outbreak of un-incidental nephrolithiasis in China children, the nephrotoxicity of melamine was paid more attention to public. 294,000 infants had been affected by melamine-contaminated formula milk by the end of November 2008. More than 50,000 infants have been hospitalized, and six deaths have been confirmed (2). Seven Asian countries and territories-Hong Kong, Japan, Macau, New Zealand, Singapore, South Korea and Taiwan had found contaminated products imported from China (3, 4). There are cases of children with nephrotoxicity related from melamine contaminated milk exposure in Taiwan (4). All evidences are pointed out that the children are the susceptibility group under high concentration exposure of melamine. In 2007, the US Food and Drug Administration (FDA) published a tolerable daily intake (TDI) for melamine of 0.63 mg/kg bw/d. World Health Organization (WHO) also published a TDI for 0.2 mg/kg bw/d and they expect to protect the children under this value. However, all estimations were based on sub-chronic animal studies. Reassessment of recommended values from USFDA and WHO are warranted for the real world children exposed to melamine. In this study, we try to build a physiologically base pharmacokinetic (PBPK) model to simulate the cumulative exposure of melamine on infants and young children. This model will assess the dose-response relationship between melamine concentration and renal toxicity. The model will also verify by the epidemiological data from investigation of Taiwan. We want to build a useful simulation model for infants and young children who are more susceptible to melamine exposure and to establish of a safe level of melamine content in infant formula by real human data.

References

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