A newly-developed analytical method for curdione and its application in concomitant toxicokinetics of reproductive toxicity studies

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Abstract

Objective: The objective of this study was to determine the toxicokinetic profile of curdione in pregnant SD rats as well as the transference of curdione into the fetus through the placental barrier system using LC-MS/MS.

Methods: A sensitive analytical method for determining the plasma concentration of curdione was developed and applied in the determination of curdione in pregnant SD rats as a simulated model. Thirteen pregnant SD rats were treated with 7, 21 and 63 mg/kg curdione once daily from GD6 to GD15. Blood samples were collected at different time points on GD6 and GD15. Maternal plasma, placental plasma, placenta tissue, amniotic fluid and fetal tissue were collected for concentration analysis after all the animals were sacrificed following one repeated dose.

Results: The results indicated that Cmax, AUC (0-t) and AUC (0-∞) increased in a dose-dependent manner both on GD6 and GD15. At 7 mg/kg group, the total serum clearance value on GD15 was reduced to approximately 16.4% of that on GD6, and the volume of distribution was also significantly decreased ($p<0.05$). Curdione could be detected in the maternal plasma, placental plasma, placenta tissue, amniotic fluid and fetal tissue, and its concentration in the fetal tissue reached saturation at 21 mg/kg.

Conclusion: It presents with the risk of toxic accumulation in the concomitant toxicokinetics of reproductive toxicity studies in SD rats and it may affect the fetus via transference through the placental barrier system.

Image

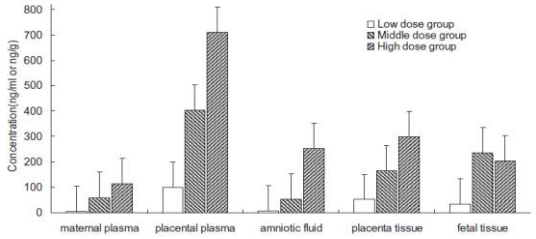

Figure: Concentration of curdione in samples from pregnant SD rats, (Mean±SD).

Recent Publications

1. Meng X, Zhang T and Sun Z Y (2015) Development and application of an analytical method for curdione quantification in pregnant Sprague-dawley rats by LC-MS/MS. Biomedical Chromatography. 29 (10): 1499-1505.

2. Meng X, Zhang T and Sun Z Y (2015) The toxicokinetic profile of curdione in pregnant SD rats and its transference in a placental barrier system detected by LC–MS/MS. Regulatory toxicology and pharmacology. 71 (2): 158-163.

3. Zhu S, Luo Y W and Sun Z Y (2016) A conjugate of methotrexate and an analog of luteinizing hormone releasing hormone shows increased efficacy against prostate cancer. Scinetific Reports (22, September). Doi: 10.1038/srep33894.

4. Ting Zhang, Ying Chen, Yang Yang,

Zhonghui Wang, Qi Pan, Sichong Xu and Zuyue Sun (2017) The potentiality of two-dimensional preantral follicle culture as an *in vitro* model in predicting premature ovarian failure. Experimental and Toxicologic Pathology. 69 (7): 477-484.

5. Wang Yong, Chen Jiao, Wu Jianhui, Zhao Yan, Pan Qi, Wang Xiu, Sun Zuyue and Zhang Yunhui (2016) Mono-2-ethyhexyl phthalate advancing the progression of prostate cancer through activating the hedgehog pathway in LNCaP cells. Toxicology *in vitro*. 32: 86-91.

Biography

Zuyue Sun is the Research Director of National Evaluation Centre for the Toxicology of Fertility Regulating Drug; a laboratory has acquired the GLP certificate of CFDA (China Food and Drug Administration). He has published more than 312 theses in China and abroad reputed journals, and 258 study projects being carried out in his laboratory.

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Notes/Comments: