**SODIUM TANSHINONE IIA SULFONATE AND SODIUM DANSHENSU OPEN THE PLACENTAL BARRIER THROUGH DOWN-REGULATION OF PLACENTAL P-GLYCOPROTEIN IN MICE: IMPLICATIONS IN THE TRANSPLACENTAL DIGOXIN TREATMENT FOR FETAL HEART FAILURE**

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*Introduction:* Placental P-glycoprotein (P-gp) plays a significant role in controlling digoxin transplacental rate. Pharmacological manipulations, such as inhibition of placental P-gp would offer the advantage of enhance digoxin availability to the fetus, while minimizing drug exposure of the mother when treating fetal heart failure with digoxin.

*Objective*: This study aimed to determine whether sodium Tan-IIA sulfonate and sodium danshensu, the main pharmacologically active components of Danshen (a widely used traditional drug during pregnancy), could inhibit placental P-gp expression and functionality or not.

*Methods*: In total, 80 pregnant C57BL mice were randomly divided intro eight groups, with 10 animals in each group: blank group, vehicle group, three sodium Tan-IIA sulfonate groups (10mg/Kg, 20mg/Kg, 40mg/Kg) and three sodium danshensu groups (10mg/Kg, 20mg/Kg, 40mg/Kg). Pregnant dams in different groups received respective intervention by intraperitoneal (i.p.) injection once daily from E9.5-E15.5. Placental abcb1a/abcb1b mRNA and P-gp protein expression were determined by real-time quantitative PCR and western-blot, respectively. Maternal plasma and fetal-unit digoxin concentrations were detected by a commercial kit assay.

*Results*: all the placental abcb1b mRNA and P-gp expression of the sodium Tan-IIA sulfonate groups and sodium danshensu groups were significantly lower than that of vehicle group with a dose dependent manner. Compared with the vehicle group, the digoxin transplacental rate was significantly higher than that of all the sodium Tan-IIA sulfonate groups and sodium danshensu groups, while there were no differences in maternal digoxin concentrations among the different groups.

*Conclusions*: Both the sodium Tan-IIA sulfonate and sodium danshensu could inhibit the placental P-gp expression and its efflux functionality. These findings suggested that danshen might be considered as an adjuvant treatment to enhance drug effectiveness when treating FCHF with digoxin, while minimizing maternal drug poisoning risk.