Application of the ERK signaling pathway inhibitor PD98059 in long-term in vivo experiments

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ABSTRACT. The aim of this study was to explore methods by which the ERK signaling pathway inhibitor PD98059 (PD) could be used in long-term in vivo experiments. Forty healthy New Zealand rabbits were randomly divided into blank control, model control, PD low-dose, PD high-dose, PD blank, dimethyl sulfoxide (DMSO) control, DMSO blank, and positive control groups. The corresponding treatments were administered to each experimental group over the course of four weeks, after which, total ERK1/2 and ERK5 protein levels, protein phosphorylation, and gene expression were measured in myocardial tissues. Treatment of rabbits with Adriamycin (doxorubicin) resulted in the significant overall differences in ERK1/2 and ERK5 phosphorylation (P < 0.05). Compared with the model control group, changes in phosphorylated ERK1/2 and phosphorylated ERK5 were lowest in the PD high-dose group (P < 0.05). No significant differences in total protein and mRNA levels of myocardial ERK1/2 and ERK5 were detected between the groups after four weeks (P > 0.05). Continuous intravenous injection of PD98059 significantly reduced phosphorylation of ERK1/2.
and that of ERK5. In conclusion, Adriamycin-induced myocardopathy and abnormal ERK signaling might constitute a valuable model for use in long-term experiments. These methods may provide a theoretical basis for related in vivo studies of long duration.

**Key words:** PD98059; ERK pathway; Signaling pathways; 
*In vivo* experiments