

Preliminary characterization of a placental factor inhibiting breathing in fetal sheep

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Abstract

Previous studies have revealed a placental extract that inhibits breathing in fetal sheep. In the present study of 29 chronically instrumented sheep at 132 ± 1 days of gestation, infusion of the 1-10 kDa extract inhibited breathing in 76% of the experiments whereas Krebs' solution inhibited it in 24%. It retained this activity after 6 months of freezing, after lyophilization, and upon lowering the pH during purification from 8.0 to 4.0, but it inhibited breathing in only 35% when the pH was lowered to 2.0. A significant dose-dependent effect was observed from a 16-fold dilution to a 4-fold concentration. Treatment of the extract with proteinase K or boiling reduced the activity to 30% or 26% inhibition, respectively. The activity was not adsorbed to an ion-exchange column at pH 7.0 or 8.0, but it was at pH 9.0 and it eluted with increasing NaCl concentrations. On a polyacrylamide gel the activity was eluted at a K_{av} of 0.66 (82% inhibition), corresponding to between 2.5 and 4.5 kDa. These findings suggest that a peptide produced by the placenta, with a molecular mass between 2.5 and 4.5 kDa, inhibits fetal breathing.

Keywords: control of breathing, umbilical circulation, placental dissection, spontaneous fetal breathing, purification and characterization.

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