Interspecies mixed effect pharmacokinetic modeling of penicillin G in cattle and swine

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Running title: pharmacokinetic modeling of penicillin G in cattle and swine

Keywords: Penicillin G, population pharmacokinetics, cattle, swine, interspecies model

Model code

```
test(){
    deriv(Aiv = - (Cl * C) + (Aim1 * Kim1)- (Cl2 * (C - C2))- (Cl3 * (C - C3)) + (Aim2 * Kim2) + (Asc * Ksc)- (QL * (C - CL))- (QK * (C - Ck))- (Qm * (C - Cm)))
    urinecpt(A0 = (Cl * C))
    deriv(Aim1 = - (Aim1 * Kim1))
    deriv(A2 = (Cl2 * (C - C2)))
    deriv(A3 = (Cl3 * (C - C3)))
    deriv(Aim2 = - (Aim2 * Kim2))
    deriv(Asc = - (Asc * Ksc))
    deriv(AL = (QL * (C - CL)) + (Apo * Kpo)- (CLL * CL))
    deriv(Apo = - (Apo * Kpo))
    urinecpt(EL = (CLL * CL))
    deriv(Ak = (QK * (C - Ck))- (CLk * Ck))
    urinecpt(Ek = (CLk * Ck))
    deriv(Am = (Qm * (C - Cm)))
    C = Aiv / V
    dosepoint(Aiv, idosevar = AivDose, infdosevar = AivInfDose, infratevar = AivInfRate)
    dosepoint(Aim1, bioavail = (Fim1), idosevar = Aim1Dose, infdosevar = Aim1InfDose, infratevar = Aim1InfRate)
    C2 = A2 / V2
    C3 = A3 / V3
    error(CEps = 1)
    observe(CObs = C + CEps)
    dosepoint(Aim2, bioavail = (Fim2), idosevar = Aim2Dose, infdosevar = Aim2InfDose, infratevar = Aim2InfRate)
```

```
dosepoint(Asc, bioavail = (Fsc), idosevar = AscDose, infdosevar = AscInfDose, infratevar = AscInfRate)

CL = AL / VL

dosepoint(Apo, bioavail = (Fpo), idosevar = ApoDose, infdosevar = ApoInfDose, infratevar = ApoInfRate)

Ck = Ak / Vk

Cm = Am / Vm

error(CEpsl = 1)

observe(CObsl = CL + CEpsl)

error(CEpsk = 1)

observe(CObsk = Ck + CEpsk)

error(CEpsm = 1)

observe(CObsm = Cm + CEpsm)

stparm(V = (tvV*(specices==0)+tvV*(specices==1))* exp(nV))

stparm(Cl = (tvCl*(specices==0)+tvCl*(specices==1)) * exp(nCl))

stparm(Kim1 = (tvKim1*(specices==0)+tvKim1*(specices==1)) * exp(nKim1))

stparm(V2 = (tvV2*(specices==0)+tvV2*(specices==1)) * exp(nV2))

stparm(Cl2 = (tvCl2*(specices==0)+tvCl2*(specices==1)) * exp(nCl2))

stparm(V3 = (tvV3*(specices==0)+tvV3*(specices==1)) * exp(nV3))

stparm(Cl3 = (tvCl3*(specices==0)+tvCl3*(specices==1)) * exp(nCl3))

stparm(Kim2 = tvKim2 * exp(nKim2))

stparm(Fim1 = tvFim1 * exp(nFim1))

stparm(Fim2 = tvFim2 * exp(nFim2))

stparm(Fsc = tvFsc * exp(nFsc))

stparm(Fpo = tvFpo * exp(nFpo))

stparm(Ksc = tvKsc * exp(nKsc))
```

```
        stparm(VL = (tvVL*(specices==0)+tvVL*(specices==1)) * exp(nVL))

        stparm(QL = (tvQL*(specices==0)+tvQL*(specices==1))  * exp(nQL))

        stparm(Kpo = tvKpo * exp(nKpo))

        stparm(CLL = (tvCLL*(specices==0)+tvCLL*(specices==1)) * exp(nCLL))

        stparm(Vk = (tvVk*(specices==0)+tvVk*(specices==1)) * exp(nVk))

        stparm(QK = (tvQK*(specices==0)+tvQK*(specices==1)) * exp(nQK))

        stparm(CLk = (tvCLk*(specices==0)+tvCLk*(specices==1)) * exp(nCLk))

        stparm(Vm = tvVm* exp(nVm))
stparm(Qm = tvQm* exp(nQm))
        covariate(specices)

        fixef(tvV = c(, 4, ))

        fixef(tvCl = c(, 105, ))

        fixef(tvKim1 = c(, 0.4, ))

        fixef(tvV2 = c(, 22, ))

        fixef(tvCl2 = c(, 24.8, ))

        fixef(tvV3 = c(, 30, ))

        fixef(tvCl3 = c(, 9.75, ))

        fixef(tvKim2 = c(, 0.22, ))

        fixef(tvFim1 = c(0, 0.8,1 ))

        fixef(tvFim2 = c(0, 0.9,1 ))

        fixef(tvFsc = c(, 0.75, ))

        fixef(tvFpo = c(, 0.5, ))

        fixef(tvKsc = c(, 0.6, ))

        fixef(tvVL = c(, 11, ))

        fixef(tvQL = c(, 25, ))
```

```
    fixef(tvKpo = c(, 0.4, ))

    fixef(tvCLL = c(, 43, ))

    fixef(tvVk = c(, 13, ))

    fixef(tvQK = c(, 25, ))

    fixef(tvCLk = c(, 42, ))

    fixef(tvVm = c(, 1, ))

    fixef(tvQm = c(, 13, ))

    fixef(dVdspecices(enable=1) = c(, 0, ))

    ranef(diag(nV, nCl, nV2, nV3, nCl2, nCl3, nKim1, nKim2, nFim1, nFim2, nFsc, nFpo, nKsc, nKpo,
nVL, nCLL, nQL, nQK, nVk, nCLk, nQm, nVm) = c(1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1))

}
```