THE USE OF THE RAT HEPATIC PORTAL VEIN TO DETERMINE VENODILATOR EFFICACY

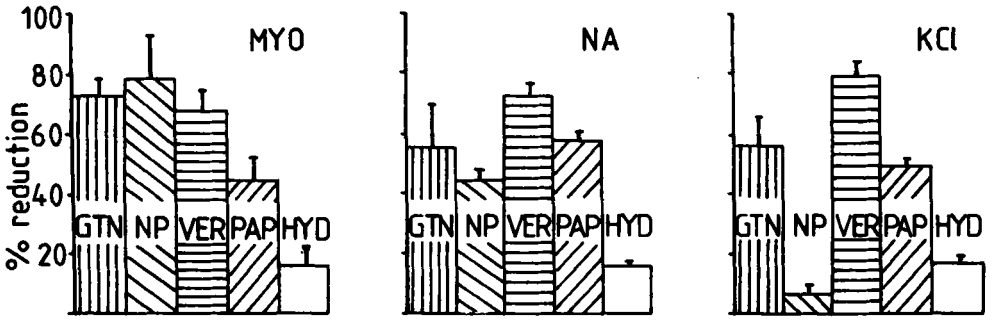
J.B. Louttit, O.A. Downing, K.A. Wilson, Department of Pharmacy, University of Aston in Birmingham, Birmingham B4 7ET.

An effective venodilator action is believed to play a significant role in the clinical usefulness of glyceryl trinitrate (GTN) in angina (Parratt 1975) and of sodium nitroprusside (NP) in heart failure (Cohn and Franciosa 1977). This work was undertaken to assess the suitability of the isolated hepatic portal vein of the rat for comparing the efficacy of drugs with venodilator actions.

Hepatic portal veins obtained from male rats (200-280g) were set up in Krebs bicarbonate solution (5.4 mM $CaCl_2$) at 37°C gassed with 5% CO_2 in O_2. Contractions of the longitudinal muscle were recorded isometrically under a resting tension of 0.5 g. NP, GTN, Verapamil (VER), Papaverine (PAP) and hydrallazine (HYD) were compared for their ability to reduce spontaneous myogenic activity (MYO) and submaximal contractions to (a) noradrenaline (NA) (3 μM) (b) KCl (60 mM) and (c) field stimulation (6 Hz).

All of the drugs with the exception of PAP caused a concentration dependent decrease in both amplitude and frequency of the spontaneous myogenic activity of the portal vein. PAP caused a decrease in amplitude but an increase in frequency. The myogenic activity was most sensitive to reduction by NP, GTN and VER and least sensitive to HYD. In contrast KCl induced contractions were most sensitive to reduction by VER but almost totally resistant to NP. (Fig. 1).

Fig. 1: The effect of vasodilators (all at 10μM) on spontaneous myogenic activity and contractions to NA (3μM) and KCl (60μM).



Human veins in vivo are most sensitive to NP and GTN, less sensitive to VER and relatively insensitive to HYD (Collier et al 1978; Robinson et al 1979). The results presented here indicate that the effect of vasodilators on the myogenic activity of rat portal vein most closely resemble the spectrum of action of these drugs on human veins in vivo with the exception of VER, which was not significantly different from NP or GTN ($P > 0.5$). The use of KCl induced contractions of portal vein to assess venodilator efficacy is considered unsuitable in view of the almost complete refractoriness to NP.

Cohn, J.N. & Franciosa, J.A. (1977) New Engl. J. Med. 297: 27-31
Collier, J.G. et al (1978) Br. J. Clin. Pharmac. 5: 34-44
Parratt, J.R. (1975) Gen. Pharmac. 6: 247-251
Robinson, B.F. et al (1979) Cardiovasc. Res. 13: 16-21.

0022-3573/81/120090P-01$02.50/0