**Summary.** Prenalterol, previously characterized as a functionally cardioselective partial β-adrenoceptor agonist, was shown to relax K⁺-elicited contractures in the uterine muscle from progesterone-pretreated rats (pD₂ 7.7) and to increase beating rate in the rat right atrium (pD₂ 8.0) at about the same concentrations with maximal effects corresponding to 94 and 82 % respectively of those of isoproterenol. Terbutaline, with equal maximal effects as isoproterenol, was 50 times more potent in the uterus (pD₂ 7.8) than in the right atrium (pD₂ 6.1). Both tissues displayed a high sensitivity to isoproterenol (pD₂ 9.1 in both tissues) indicating large receptor reserves for the full agonist.

The maximal relaxing effect of prenalterol in the uterus was obtained at about a three-fold increase of the cyclic AMP content, which is similar to that obtained with isoproterenol at a corresponding relaxation.

The effects in the uterine muscle of all three agonists were mediated through β₂-adrenoceptors since β₂-adrenoceptor blockers (ICI 118,551 and IPS 339) antagonized the effects in concentrations which had only marginal effects on the atrial responses of the agonists. The β₁-agonists pafenolol and pirmatolol in concentrations higher than those, which blocked the effects of the agonists on beating rate, were devoid of inhibitory effects in the uterus.

These results indicate that prenalterol possesses the ability to elicit a functional response by stimulation of either β₁- or β₂-adrenoceptors provided that the tissue has a large spare receptor reserve for full agonists.

**Key words:** Prenalterol -- Agonistic activity -- β-Adrenoceptors -- Spare receptors -- Cyclic AMP

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**Methods**

*Isolated Rat Uterine Muscle.* Female Sprague Dawley rats (200–240 g) were pretreated with progesterone (10 mg/kg/day i.m.) for 4 days before the experiments. The animals were killed by cervical dislocation and the uterine horns were dissected out, freed from surrounding tissue and cut open. Each horn (length 1.5 cm) was mounted in an organ bath (50 ml) with one end fixed and the other end sutured to a Grass force displacement transducer (FT03). The bathing fluid was an aerated (95 % O₂ and 5 % CO₂) Krebs solution (37°C) of the following composition in mM: NaCl 122, KCl 4.7, CaCl₂ 2.5, MgCl₂ 1.3, NaHCO₃ 15.4, KH₂PO₄ 1.2, disodium calcium EDTA 0.04 and glucose 11.1 (pH 7.4).

The preparation was stretched to a passive pretension of 0.5 g which usually stabilized at a baseline tension of 0.35—
The uterine horns were weighed and homogenized in 10 ml of ice-cold Tris-isosaline (20 gM Tris in 0.154 M NaCl, pH 7.4). As indicated above, the rat uterus was excised and placed in 0.25 ml. Binding assays were routinely carried out as described previously (Hedberg et al. 1980b; Hedberg and Mattsson 1981).

The dissociation constant ($K_d$) for IHPY and the density of $\beta$-adrenoceptors ($B_{max}$) were determined in each uterus preparation by analysis of the amount of specifically-bound IHPY at nine concentrations of the radioligand (15–400 pM) according to the method of Scatchard (1949).

To determine the affinities of isoproterenol and prenalterol for $\beta$-adrenergic receptors in the uterus muscle the inhibition of specific IHPY binding, expressed in percent of maximal inhibition by 20 $\mu$M isoproterenol, was determined following incubation with various concentrations of the agonists. $K_a$ values for the inhibition of IHPY binding by isoproterenol and prenalterol were calculated using the method of Cheng and Prusoff (1973). The affinity values of these compounds are expressed as the negative logarithm of the dissociation constants ($pK_a$).

**Protein Determination.** Protein was determined using the method of Lowry et al. (1951).

**Isolated Rat Right Atrium.** Female Sprague Dawley rats (200–240 g) were killed by cervical dislocation, and the hearts were rapidly removed and washed in aerated (95% O$_2$ and 5% CO$_2$) buffer (pH 7.4) containing in mM: NaCl 122, KCl 4.7, CaCl$_2$ 2.5, MgCl$_2$ 1.3, NaHCO$_3$ 24.9, KH$_2$PO$_4$ 1.2, disodium calcium EDTA 0.04 and glucose 11.1. The right atrium was dissected free from surrounding tissue and mounted for recording of contractions as described above. The solution in the organ bath (50 ml) of the above composition was kept at 32°C. The resting tension (0.2 g) was just sufficient for recording of contractions. The heart rate (HR) was recorded with a cardiotachometer (Grass model 7P4F) which was triggered by the contraction signal. The preparations were incubated with phenoxybenzamine (10$^{-6}$ M) for 30 min. After repeated washing and equilibration, concentration effect curves were constructed as described above for the uterine muscle preparation. In order to establish the maximal chronotropic responses in each preparation, high concentrations of isoproterenol were added immediately after the maximal effects of prenalterol or terbutaline had been obtained.

**Chemicals.** Prenalterol (1-(4-hydroxyphenoxy)-3-isopropylamino-2-propanol hydrochloride = (–)-H 80/62 = H 133/22 = CGP 7760/B), pamatolol (methyl(+)-[p-[2-hydroxy-3-(isopropylamino) propoxy]-phenylethyl]carbamatesulphate, H 104/08) and pafenolol ([+]-N-2(4-[2-hydroxy-3-isopropylaminoxy]phenylethyl-N'-isopropylurea, H 138/03) were from AB Hässle and terbutaline (1-(3,5-dihydroxyphenyl)-2-(t-butyloxamo)-ethanolsulphate) was from AB Draco.

The gifts of the following chemicals are acknowledged: ICI 118,551 (erythrole-DL-1-(7-methylindan-4-yl oxy)-3-isopropylaminobutan-2-olhydrochloride) and propanolol hydrochloride from ICI Ltd, England, IPS 339 (t-butyl-amino-3-ol-2-propyl)oximino-9-fluorene-p-hy-