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## Product Data Sheet

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### Animal experiment:

Guinea-pigs[3]PACAP-27 (0.045 to 4.5 nmol/kg/min), salbutamol (0.045 to 4.5 nmol/kg/min) or sterile saline is given i.v. (1.0 mL) via an infusion pump, starting 5 min before and continuing 10 min after airway challenge[3].Dogs[4]Four dogs (28.4±1.8 kg) receive PACAP (1-27) with four different concentrations of 0.01, 0.1, 1.0 and 10 µg/mL, or 0.00318, 0.0318, 0.318 and 3.18 µM, respectively. Each solution is locally infused at a rate of 0.5 mL/min for precisely 1 min. A total dose delivered to the pancreas during each infusion is therefore 0.005, 0.05, 0.5 and 5 µg. The dead volume of the pancreatic arterial catheter (0.5 mL) is taken into account in relation to the infusion rate. After taking the initial control sample, simultaneously from the SPD vein and the aorta, saline is infused for 1 min and samples are obtained 1, 3 and 5 min after the onset of infusion. This procedure is repeated every 15 min for the doses of PACAP (1-27). The sample obtained at 15 min after the onset of each infusion served as control for the subsequent intervention[4].

### References:

- [1]. Gourlet P, et al. Fragments of pituitary adenylate cyclase activating polypeptide discriminate between type I and II recombinant receptors. Eur J Pharmacol. 1995 Dec 4;287(1):7-11.
- [2]. Schäfer H, et al. Structural motifs of pituitary adenylate cyclase-

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activating  
polypeptide  
(PACAP) defining  
PAC1-receptor  
selectivity. Regul  
Pept. 1999 Feb  
5;79(2-3):83-92.  
[3]. Lindén A, et al.  
Inhibition of  
bronchoconstriction  
by pituitary  
adenylate cyclase  
activating  
polypeptide (PACAP  
1-27) in guinea-  
pigs in vivo. Br J  
Pharmacol. 1995  
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### Background

PACAP (1-27), human, ovine, rat (PACAP 1-27) is the N-terminal fragment of PACAP-38, and is a potent PACAP receptor antagonist with IC<sub>50</sub>s of 3 nM, 2 nM and 5 nM for rat PAC1, rat VPAC1 and human VPAC2, respectively[1].

Radioligand receptor binding assays with I-monoiodinated PACAP (1-27), human, ovine, rat confirms the presence of PAC -receptors on AR4-2J cells, since PACAP (1-27), human, ovine, rat and PACAP(1-38) equipotently displaces radioligand binding with a K<sub>d</sub> of 1-2 nM, whereas vasoactive intestinal peptide (VIP) is 1000-fold less potent. PACAP (1-27), human, ovine, rat exhibits a distinct and much higher susceptibility to VIP-amino acid substitutions. PACAP (1-27), human, ovine, rat has potency and binding affinity to stimulate IP<sub>3</sub> and cAMP formation in AR4-2J cells[2].

The inhibitory effect of pituitary adenylylating polypeptide (PACAP (1-27), human, ovine, rat) on the increase in total pulmonary resistance (RL) caused by allergen or histamine in anaesthetized, ventilated guinea-pigs is studied. PACAP (1-27),

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human, ovine, rat given via i.v. infusion (0.045-4.5 nmol/kg/min) dose-dependently reduces the increase in RL caused by inhaled ovalbumin and histamine. At the highest dose, PACAP (1-27), human, ovine, rat prevented the increase in RL caused by ovalbumin and histamine completely. Infusion of PACAP (1-27), human, ovine, rat and the  $\beta$ 2-adrenoceptor agonist, salbutamol (0.045-4.5 nmol/kg/min) inhibit the increase in RL similarly, but salbutamol increases the heart rate more than PACAP (1-27), human, ovine, rat[3].

### References:

- [1]. Gourlet P, et al. Fragments of pituitary adenylate cyclase activating polypeptide discriminate between type I and II recombinant receptors. *Eur J Pharmacol.* 1995 Dec 4;287(1):7-11.
- [2]. Schäfer H, et al. Structural motifs of pituitary adenylate cyclase-activating polypeptide (PACAP) defining PAC1-receptor selectivity. *Regul Pept.* 1999 Feb 5;79(2-3):83-92.
- [3]. Lindén A, et al. Inhibition of bronchoconstriction by pituitary adenylate cyclase activating polypeptide (PACAP 1-27) in guinea-pigs in vivo. *Br J Pharmacol.* 1995 Jul;115(6):913-6.

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