THE CGRP-ANTAGONIST BIBN4096BS DISCRIMINATES BETWEEN THE ACTION OF α - AND β -CGRP *IN VITRO*

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Calcitonin gene-related peptide (CGRP) is a potent vasodilatory peptide implicated in migraine pathogenesis. Two protein isoforms, α - and β -CGRP, have been described and it has been reported that the two isoforms might activate two discrete CGRP receptor subtypes[1]. Recently, we showed that the nonpeptide CGRP antagonist BIBN4096BS can discriminate between putative CGRP-1 and CGRP-2 receptors in atrial and vas deferens tissue[2]. These data suggest that BIBN4096BS could be a useful tool in further characterizing CGRP-receptor heterogeneity. Therefore, in the present study we address the effects of BIBN4096BS on the action of α - and β -CGRP in four different tissues. Rat atria and vasa deferentia were employed as bioassays for CGRP-1 and -2 receptors, respectively. Results show that in rat atrium BIBN4096BS did not discriminate between effects of human α - and β -CGRP ($pK_B = 8.52$ and 8.13). Similar results were obtained for h α - and h β -CGRP in the vas deferens ($pK_B = 7.11$). Interestingly, in pig cerebral and coronary arteries BIBN4096BS did discriminate between the action of h α and h β -CGRP ($pK_B = 8.08/8.0$ and $6.75/6.6$) indicating a stronger inhibitory effect of BIBN4096BS on α -CGRP dilatory action compared to β -CGRP in the arteries. In conclusion, our results demonstrate BIBN4096BS as a highly potent and selective tool revealing CGRP-receptor heterogeneity.

REFERENCES

1. Jansen, I. (1992) Neuropeptides 21, 73–79.
2. Wu, D. et al. (2000) Eur. J. Pharmacol. 400, 313–319.