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 hα- and hβ-CGRP in the vas deferens (pK_B = 7.11). Interestingly, in pig cerebral and coronary arteries BIBN4096BS did discriminate between the action of hα and hβ-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