분류번호	Ⅲ-P-59

Excitatory effect of KR-25018 and capsaicin on the isolated guinea pig bronchi

정이숙°, 신화섭*, 박노상*, 문창현, 조태순†
아주대 의대, *한국화학연구소, †성균관대 약대

We investigated the peripheral excitatory effect of capsaicin and KR-25018, a newly synthesized capsaicin derivative which was demonstrated to have a potent analgesic activity. KR-25018 and capsaicin were found to be both potent efficacious contractors of isolated guinea pig bronchial smooth muscle. KR-25018 was equipotent with capsaicin and [Sar^9,$Met(O_2)^{11}$]-substance P, 10-fold more potent than histamine and 10-fold less potent than [β-Ala^8]-neurokinin A(4-10), and their -log(M)EC_{50} values were 6.94±0.08, 6.86±0.05, 6.96±0.07, 5.64±0.04, 7.96±0.02, respectively. Contractile responses to KR-25018 and capsaicin were potentiated by phosphoramidon (1 μM), an inhibitor of neuropeptide-inactivating endopeptidase, but completely abolished in a calcium-free medium. These responses to KR-25018 and capsaicin were unaffected by the NK-1 antagonist CP96345 (1 μM), partially inhibited by the NK-2 antagonist SR48968 (1 μM) but almost completely abolished by a combination of the antagonists. A vanilloid receptor antagonist capsazepine competitively antagonized the responses to both KR-25018 and capsaicin (pA_2: aganst KR-25018, 5.98±0.47; against capsaicin, 5.80±0.31), and a capsaicin-sensitive cation channel antagonist ruthenium red caused significant reduction in the maximum responses to KR-25018 and capsaicin (pD'_2: against KR-25018, 4.61±0.33; against capsaicin 4.96±0.21). In conclusion, the present results suggest that KR-25018 and cpasaicin act on the same vanilloid receptor inducing the influx of calcium through ruthenium red-sensitive cation channel and produce contractile responses via the release of tachykinins that act on both NK-1 and NK-2 receptor subtypes.