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LIGAND BINDING CHRATERISTICS OF K_2- OPIOID RECEPTOR AND ITS ROLE IN REGULATION OF [^{3}H]HISTAMINE RELEASE IN FRONTAL CORTEX OF THE RAT

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It has been shown that there are several subtypes of κ opioid receptor. We have evaluated the properties of non-μ, non-δ binding of [^{3}H]DIP, a nonselective opioid antagonist, in rat cortex membranes. Binding to μ and δ sites was inhibited by the use of an excess of competing selective agonists (DAMGO, DPDPE) for these sites. (-)Ethylketocyclazocine(EKC) inhibited [^{3}H]DIP binding with Ki of 70 nM. However, arylacetamides (U69593 and U50488H) gave little inhibition. Also, we have examined the opioid modulation of K^+(30 mM)-induced histamine release in rat frontal cortex slices labeled with l-[^{3}H]histidine. The [^{3}H]histamine release from cortex slices was inhibited by EKC, a κ_1-and κ_2-agonist, in a concentration-dependent manner(10 to 10,000 nM). The IC_{50} of EKC was 107 ± 6 nM. However, the δ receptor selective agonists, DPDPE and deltorphine II, μ receptor agonists, DAMGO and TAPS, κ_1-agonists, U69593 and U50488H, and ε-agonist, β-endorphin, did not inhibit histamine release even in micromolar dose, indicating that μ, δ or κ_1 receptors are not involved. The concentration-response curve of EKC was shifted to right in the presence of naloxone (300 nM), a μ preferential antagonist, nor-binaltorphimine(300 nM), a κ_1 preferential antagonist and bremazocine(1 nM), a κ_1-agonist and κ_2-antagonist. These results suggest that κ_2 opioid receptor regulates histamine release in the frontal cortex of the rat. (This work is supported in part by Basic Medical Science Fund, Korea Research Foundation to KWK, 1993.)