LIGAND BINDING CHRATERISTICS OF $\kappa_2$- OPIOID RECEPTOR AND ITS ROLE IN REGULATION OF $[^{3}\text{H}]$HISTAMINE RELEASE IN FRONTAL CORTEX OF THE RAT

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It has been shown that there are several subtypes of $\kappa$ opioid receptor. We have evaluated the properties of non-$\mu$, non-$\delta$ binding of $[^{3}\text{H}]$DIP, a nonselective opioid antagonist, in rat cortex membranes. Binding to $\mu$ and $\delta$ sites was inhibited by the use of an excess of competing selective agonists (DAMGO, DPDPE) for these sites. ($^{\sim}$Ethylketocyclazocine(EKC) inhibited $[^{3}\text{H}]$DIP binding with Ki of 70 nM. However, aryacetamides (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 $[^{3}\text{H}]$histidine. The $[^{3}\text{H}]$histamine release from cortex slices was inhibited by EKC, a $\kappa_1$-and $\kappa_2$-agonist, in a concentration-dependent manner(10 to 10,000 nM). The IC$_{50}$ of EKC was 107 ± 6 nM. However, the $\delta$ receptor selective agonists, DPDPE and deltorphine II, $\mu$ receptor agonists, DAMGO and TAPS, $\kappa_1$-agonists, U69593 and U50488H, and $\epsilon$-agonist, $\beta$-endorphin, did not inhibit histamine release even in micromolar dose, indicating that $\mu$, $\delta$ or $\kappa_1$ receptors are not involved. The concentration-response curve of EKC was shifted to right in the presence of naloxone (300 nM), a $\mu$ preferential antagonist, norbinaltorphimine(300 nM), a $\kappa_1$ preferential antagonist and bremazocine(1 nM), a $\kappa_1$-agonist and $\kappa_2$-antagonist. These results suggest that $\kappa_2$ 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.)