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| 제 목 | CLASSIFICATION OF MUSCARINIC RECEPTOR SUBTYPES BY OXOMEMAZINE |
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The binding characteristic of oxomemazine to muscarinic receptor in the cerebrum, heart, and ileum were compared to those of pirenzepine to investigate whether oxomemazine could classify the muscarinic receptor subtypes. [$^3$H]Quinuclidinyl benzilate(QNB) identified a single class of muscarinic receptors with apparent $K_D$ value of about 60 pM in three tissues. Analysis of the pirenzepine inhibition curve of [$^3$H]QNB binding to cerebral microsome indicated the presence of two receptor subtypes with high (Ki=16 nM, $M_1$-receptor) and low (Ki=400 nM, $M_2$-receptor) affinity for pirenzepine. Oxomemazine also identified two receptor subtypes with high (Ki=84 nM, $O_H$-receptor) and low (Ki=1.4 μM, $O_L$-receptor) affinity in rat cerebral microsome. The percentage population of the $M_1$-and $M_2$-receptors to the total receptors were 61:39, and those of the $O_H$- and $O_L$-receptors 39:61, respectively. However, the Hill coefficients of these two drugs for the inhibition of [$^3$H]QNB binding to the heart and ileum were close to unity which indicated that these drugs bound to a uniform population of receptors in these two tissues. The Ki values for the low affinity sites of pirenzepine and oxomemazine in the cerebrum were similar to those of these drugs in the heart ileum. Both pirenzepine and oxomemazine increased $K_D$ value for [$^3$H]QNB without affecting the binding sites concentration and Hill coefficient for the [$^3$H]QNB binding. Oxomemazine had a 10-fold lower affinity at $M_2$-receptors than at $M_1$-receptors, and pirenzepine a 8-fold lower affinity at $O_L$-receptors than OH-receptors. Analysis of the shallow competition curves of oxomemazine for the $M_1$ receptors and pirenzepine for the $O_L$-receptors yielded that 69% of the $M_1$-receptors were of the $O_H$-receptors and the remaining 31% of the $O_L$-receptors, and that 29% of the $O_L$-receptors were of the $M_1$-receptors and 71% of the $M_2$-receptors. However, $M_2$ for oxomemazine and $O_H$ for pirenzepine were composed of a uniform population. These results suggest that oxomemazine could discriminatethe muscarnic receptor subtypes and may subclassify the $M_1$-receptors into two subtypes.