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Anxiolytic-Like Effect of CBPharm-001 and Its Possible Molecular Mechanisms

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Diazepam is widely used for the treatment of anxiety. CBPharm-001 has similar structure with diazepam, and related compounds of CBPharm-001 were introduced to have anxiolytic-like effect. This experiment was performed to investigate the anxiolytic-like effect of CBPharm-001 and possible anxiolytic molecular mechanisms. At one time oral administration of CBPharm-001 (0.2, 0.5, 1 mg/kg) significantly increased the number of open arm entries and the spent time on open arm compared with these of vehicle or diazepam (2 mg/kg) group in the elevated plus maze. This effect (1 mg/kg) was similar extend of diazepam (2 mg/kg) treated group. Locomotor activity, whereas, was dose-dependently decreased by CBPharm-001 as diazepam did. Flumazenil, a GABAA receptor antagonist (benzodiazepine site), abrogated CBPharm-001-induced open arm entries number and spent time. CBPharm-001 reversed antagonistic effect of Flumazenil. CBPharm-001 selectively increased the GABAA-α1 subunit expression in amygdala. In additional, binding assay experiments using [^{3}H]-flunitrazepam showed that CBPharm-001 bound to GABAA receptor (benzodiazepine site) by competition with diazepam. Moreover, in IMR-32 human neuroblastoma cells and neuronal primary culture cell, 10, 20 and 50 μM of CBPharm-001 significantly increased Cl- influx. These results showed that CBPharm-001 has an anxiolytic-like effect, and this pharmacologic effect may be related with GABAA receptor-activated Cl channel opening.

Keyword: anxiolytic-like effect, Benzodiazepine site