

Antidepressant-Like Effects of EQC-34, a 5HT₃ Receptor Antagonist in Neurobehavioral Mouse Model of Depression

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Abstract : Depression is among the leading causes of death worldwide. The current pharmacotherapy is associated with poor compliance, resistance and relapse, which necessitate the development of novel compounds with better efficacy. The present study designed and synthesized EQC-34 (N-cyclohexyl-3-ethoxyquinoxalin-2-carboxamide) as novel serotonin type-3 (5HT₃) antagonist and evaluated its antidepressant-like effects using neurobehavioral mouse model. 5HT₃ antagonism (as pA₂ value) was determined on the longitudinal smooth muscle of guinea-pig ileum against 2-methyl-5HT (a 5HT₃ agonist). The doses were calculated by dose response of basal locomotor activity. Consequently, effects of EQC-34 on neurobehavioral parameters were measured in forced swim (FST) and tail suspension test (TST). The possible mechanism was estimated by interaction study with fluoxetine (a selective serotonin reuptake inhibitor) and mCPBG (1-(m-chlorophenyl)-biguanide, a selective 5HT₃ agonist), and confirmed by potentiation of head twitch response by 5hydroxy-L-tryptophan (5HTP). EQC-34 (1-4 mg/kg, i.p.) produced significant decreased behavioral despair effects in FST and TST. It potentiated fluoxetine response, while mCPBG reduced EQC-34 activity in FST. Further, EQC-34 potentiated 5HTP induced head twitch response. EQC-34 revealed potential antidepressant-like effects, which may involve 5HT₃ receptor mediated facilitation of 5HT neurotransmission, thereby reversing the pathological deficiency of monoamines (5HT) observed in depression. Thus, it may be further investigated as promising agent to improve therapeutics of depression.

Keywords : depression, forced swim test, 5HT₃ receptor antagonist, serotonin

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