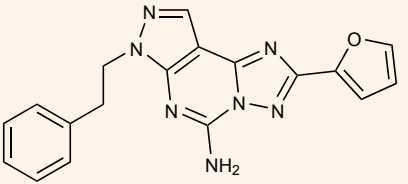
SCH 58261: A potent and selective non-xanthine A_{2A} adenosine receptor antagonist

Adenosine (Prod. No. A 9251) acts as a modulator of neuronal activity through its interaction with four receptor subtypes referred to as A_1, A_{2A}, A_{2B} and A_3. Activation of these receptors can protect neurons from damage caused by ischemia and excitotoxins [1]. Adenosine also has the ability to reduce the release of several neurotransmitters, including **glutamate** (Prod. No. G 1251).

Sigma-RBI is now pleased to offer **SCH 58261** (Prod. No. S 4568), a potent and selective A_{2A} adenosine receptor antagonist. This compound displayed affinity in the low nanomolar range at A_{2A} adenosine receptors using [^{3}H]-CHA and [^{3}H]-CGS 21680 as radioligands as well as 50 to100-fold A_{2A} vs A_1 selectivity in rat and bovine brain tissues [2]. In functional assays, SCH 58261 competitively blocks the effects induced by **CGS 21680** (Prod. No. C-141), an A_{2A} selective agonist, with pA_2 values of 7.9 in a rabbit platelet aggregation assay and 9.5 in a porcine coronary artery relaxation assay. The compound failed to block responses mediated by A_{2B} adenosine receptors in similar studies [2].

SCH 58261 has been shown to protect against neuronal cell death produced by ischemia or excitotoxicity [1]. Thus, when administered to rats that had undergone middle cerebral artery occlusion, SCH 58261 suppressed turning behavior and significantly reduced the release of glutamate, **aspartate** (Prod. No. A 9256), **GABA** (Prod. No. A 2129), adenosine and **taurine** (Prod. No. T 0625) [3]. These results suggest a neuroprotective effect of this compound. In another study, the role of A_1 and A_{2A} adenosine receptors in controlling the rise of extracellular glutamate during ischemia was investigated by monitoring the effects of selective A_1 and A_{2A} adenosine receptor antagonists on ischemia-evoked glutamate release in rat cerebrocortical slices. SCH 58261 decreased [^{3}H]-D-aspartate or endogenous glutamate efflux (50% and 55% inhibition, respectively) displaying EC_{50} values of 14.9 nM and 7.6 nM, respectively. This study also indicates that SCH 58261 is effective if administered during ischemia [4].

SCH 58261 is therefore an important new tool for studying A_{2A} adenosine receptors and their role in various diseases.



SCH 58261
(Prod. No. S 4568)

References

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