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Possible Purinergic Mediation of Anxiolytic Effect of Carbamazepine Measured in the Conflict Test with Rats

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SUMMARY. Using a modified Geller and Seifter test in rats the mechanisms of anticonflict effect of carbamazepine was investigated. The purinoceptor antagonist aminophyline (5 mg/kg) blocked the carbamazepine effect in this paradigm. On the other hand, papaverine (5 mg/kg) significantly increased the punished responses, as observed with anxiolytic drugs which indicates an anticonflict effect for this drug. Carbamazepine (2.5 mg/kg) and papaverine (2.5 mg/kg) when administered in combination with doses which had no effects by themselves, showed statistically significant increase on punished responding. Therefore, these results provide preliminary evidence suggesting that carbamazepine acts in the anticonflict effect through its action on purinoceptors.

RESUMEN. "Posible Mediación Purinérgica del Efecto Ansiolítico de Carbamazepina medida por medio del Test de Conflicto en Ratas". Se investigó en ratas el mecanismo del efecto "anticonflicto" de la carbamazepina, empleando una pueba de Geller y Seifter modificada. El antagonista purino-receptor aminofilina (5 mg/kg) bloqueó en este paradigma el efecto de la carbamazepina. Por otra parte la papaverina (5 mg/kg) aumentó significativamente las respuestas al castigo, como se observa con los fármacos ansiolíticos, lo que muestra su efecto "anticonflicto". Cuando se administraron la carbamazepina y la papaverina en combinación, a dosis de 2,5 mg/kg, respectivamente, se observó un aumento significativo en la respuesta al castigo. Los resultados proporcionan evidencia preliminar de que la carbamazepina actúa a través de su acción sobre los purino-receptores.

INTRODUCTION

Although classified as an antiepileptic agent, used in the treatment of complex partial epilepsy and generalized tonic-clonic seizures, carbamazepine (CBZ) is also effective in two animal models of anxiety, which are predictive of clinical anxiolytic drug action [1,2].

Adenosine or related nucleotides may present sedative and anticonvulsant properties when administered peripherally or centrally to mammals [3-5]. This purine has also hypnogenic properties and when given at high doses it presents anti-nociceptive action [6]. *In vitro,* adenosine agonists are potent modulators of adenylate cyclase activity and of neurotransmitter release [7]. In general, these effects of adenosine can be antagonized by the alkylxanthine compounds such as caffeine, theophylline and aminophylline (AMN), which could act as adenosine-receptor antagonists in the central nervous system [8].

A previous study, showed that CBZ reduced the effect of 1-methyl-isoguanosine, an adenosine agonist, in the isolated guinea pig ileum. It was also demonstrated that theophylline, an adenosine antagonist, significantly decreased the anticonvulsant effect of CBZ. These results suggest that the pharmacological effect of CBZ could be the result of interference of this drug in the adenosine-mediated neurotransmission [9,10].

In the present study we evaluated whether the anticonflict effect of CBZ may be affected by

KEY WORDS: Adenosine-mediated neurotransmission, Aminophylline, Anxiolytic activity, Carbamazepine, Conflict-test, Papaverine.
PALABRAS CLAVE: Actividad ansiolítica, Adenosina, Aminofilina, Carbamazepina, Papaverina, Test del conflicto.

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