

Evaluation of seizure activity after Phospho-Diesterase-7 Inhibition with Guanylate cyclase activation and inhibition in animal model of epilepsy

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The role of soluble guanylate cyclase (GC) activator (A-350619) and inhibitor (methylene blue) was evaluated in the presence of phosphodiesterase-7 (PDE-7) inhibitor such as BRL-50481, in a animal model of epilepsy. Seizures were induced in the animals by subjecting them to an injection of chemical convulsant, pentylenetetrazole (PTZ). The study mainly comprises the onset of seizures, mortality/recovery, percentage of prevention of seizures (anti-convulsant) and total duration of convulsive time. The combination of methylene blue with BRL 50481 showed a delay in onset ($P<0.001$) and in incidence of seizures, compared to A-350619 and BRL 50481 alone treated group. The total convulsive time was reduced significantly ($P<0.01$) in methylene blue alone treated

(69.2%) groups, compared to DMSO treated group (100%). The study also demonstrates that methylene blue *per se* and methylene blue with BRL 50481 greatly increased the anti-convulsant activity ($P<0.01$ and $P<0.05$) along with higher protection 83.3% and 66.7% range respectively in PTZ model. A-350619 and Methylene blue were also able to activate and inhibit respectively the whole brain cGMP levels of the rat as measured by radioimmunoassay. The present results suggested of the possible involvement of guanylate cyclase enzyme in presence of phosphodiesterase-7 inhibition, delaying the onset of seizure activity as well as prolonging the total duration of convulsive time in PTZ induced model.