

## Anti-inflammatory effects of clavulanic acid in carrageenan induced paw edema in rats

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The present study was designed to evaluate the anti-inflammatory effects of Clavulanic acid, as a GCPII inhibitor on carrageenan-induced paw edema in rats. Clavulanic acid was administered intra-peritoneally (100, 200 and 300 mg/kg) 20 min before the subplantar injection of carrageenan. Neutrophil infiltration (MPO activity), lipid peroxidation (MDA assay), free radical scavenging activity (GPx and SOD assay), IL1 $\beta$ , TNF- $\alpha$  and PGE2 levels were assessed in the paw tissue of Clavulanic acid treated rats compared to control rats. Results showed that i.p. administration of Clavulanic acid (200 and 300 mg/kg i.p.) considerably reduced maximum paw volume by 54.51 % and 59.81% and total inflammatory response (AUC) by 53.17% and 59.13% four h after induction of inflammation (P<0.001). Injection of Clavulanic acid (200 and 300 mg/kg i.p.) led to a marked reduction of MPO activity in inflamed paw by 79% and 82% in comparison with control group (P<0.01). Moreover, Clavulanic acid reduced the MDA levels to 53.22%. Levels of IL-1 $\beta$ , TNF- $\alpha$  and PGE2 in Clavulanic acid (300 mg/kg i.p.) treated groups were respectively reduced by 61.21%, 35.15% and 13.28%. Generally, Inhibition of the GCPII by Clavulanic acid increases the levels of NAAG and decreases the levels of glutamate. Overall, our results suggest that NAAG activation of mGlu3 receptors on sensory neurons and reduction of glutamate level in peripheral terminals negate the effects of PGE2 and reduces sensory neuron communication of inflammation.

**Keywords:** Glutamate; Inflammation; Carrageenan; Cytokines