

Evaluating the effects of A-803467, a selective Nav_v1.8 blocker, on cough response in guinea pigs with allergic rhinitis

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Introduction: Chronic cough, often linked to conditions like allergic rhinitis (AR), significantly impacts daily life. It arises from the dysregulation of the cough reflex due to inflammatory mediators affecting sensory nerves. Current antitussives are often ineffective and have negative side effects. This study evaluates the effect of the Nav_v1.8 blocker A-803467 on cough in guinea pigs with an AR model.

Methods: Dunkin-Hartley guinea pigs were sensitised with ovalbumin (OVA) and challenged intranasally for six weeks in 7-day intervals with subsequent monitoring of AR symptoms. Cough was induced by inhalation of citric acid aerosol (0.4M) before nasal challenge (NCH) (baseline values), then one hour after the NCH. On the 4th and 6th NCH, the tested OVA-inhibitor group was pre-treated with an inhaled Nav_v1.8 blocker (A-803467, 3mM, 10min) before tussigen inhalation.

Results: Chronic AR increased the cough response to citric acid compared to controls (10.95±1.15 vs. 6.10±1.15, P=0.0147, n=10 each). Pre-treatment with the Nav_v1.8 blocker significantly reduced the cough reflex by approximately 72% (3.05±0.36 vs. 10.95±1.15, P<0.0001) without any changes in respiratory rate.

Conclusion: These findings suggest that Nav_v1.8 channels may serve as a promising target for developing effective antitussive therapy.

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