Abstract:
Background: The aim of our study was (1) the pharmacological characterization of EP3 receptors in human pulmonary arteries and (2) the examination of the potential involvement of these receptors in the regulation of neurogenic tachycardia in pithed rats.

Methods: Experiments were performed on isolated human pulmonary arteries and pithed rats.

Results: The prostanoid EP3 receptor agonist sulprostone (1 nM – 100 µM) concentration-dependently contracted isolated human pulmonary arteries (pEC50 6.88 ± 0.10). The EP3 receptor antagonist SC 19920 (100 µM) did not affect the vasoconstriction induced by sulprostone, the TP receptor antagonist sulotroban (10 µM) only slightly attenuated the effects elicited by sulprostone > 3 µM, whereas L-826266 (10 µM) shifted its concentration-response curve to the right (apparent pA2 value 6.18; incubation time 0.5 h). In rings exposed to L-826266 (0.1, 1 or 10 µM) for 3 h, a concentration-dependent inhibitory effect against the sulprostone-induced vasoconstriction was obtained, yielding a Schild plot-based pA2 value of 7.39. In pithed rats, sulprostone (10 – 1,000 nmol/kg), but not the IP/EP3 receptor agonist iloprost (1–100 nmol/kg), inhibited the electrically evoked increase in heart rate (HR) dose-dependently, maximally by at least 80%. L-826266 (3 µmol/kg) did not affect basal HR and diastolic blood pressure, but reduced the inhibitory effect of sulprostone 1,000 nmol/kg by about 20%.

Conclusion: EP3 receptors (1) located postsynaptically strongly contract human pulmonary arteries and (2) located presynaptically on sympathetic nerve fibers supplying the heart of pithed rats strongly inhibit the neurogenic tachycardia.

Key words:
EP3 receptors, L-826266, human pulmonary artery, neurogenic tachycardia, pithed rats