

## EVIDENCE FOR ANTITUSSIVE EFFECTS OF NASAL THYMOL CHALLENGES IN HUMAN HEALTHY VOLUNTEERS

S. Gavliakova<sup>1</sup>, Z. Biringerova<sup>1,2</sup>, T. Buday<sup>1</sup>, M. Brozmanova<sup>1</sup>, V. Calkovsky<sup>3</sup>, I. Poliacek<sup>4</sup>, J. Plevkova<sup>1</sup>.

<sup>1</sup>Department of Pathophysiology, Jessenius Faculty of Medicine, Comenius University, Sklabinska 26, 03601 Martin, Slovakia, [silvia.gavliakova@fmed.uniba.sk](mailto:silvia.gavliakova@fmed.uniba.sk); <sup>2</sup>KIAIM, <sup>3</sup>Department of Otorhinolaryngology, <sup>4</sup>Department of Medical Biophysics, Jessenius Faculty of Medicine, Comenius University, Martin, Slovakia

Common cold and seasonal upper airway viral infections are usually accompanied by cough, and it was already documented that cough reflex sensitivity rises during such diseases and goes back to pre-disease values after recovery. Antipyretics, over-the-counter drugs and aromatherapy are commonly used to attenuate upper airway symptoms. Common cold and seasonal upper airway viral infections are usually accompanied by cough, and it was already documented that cough reflex sensitivity rises during such diseases and goes back to pre-disease values after recovery. Antipyretics, over-the-counter drugs and aromatherapy are commonly used to attenuate upper airway symptoms and coughing. Menthol, eucalyptol, thymol, and other aromatic substances are frequently used in these drugs based on empirical approach. We already documented that nasal administration of menthol drops has antiirritative and cough suppressing effect in humans. Now we focused on thymol. Extract of thyme – phenol with characteristic smell, which has documented antibacterial, antifungal and antioxidative activity. In respiratory system it is known to modulate mucocilliary transport, has indirect effect on airway  $\beta_2$  receptors and has beneficial effect on cough in children with acute bronchitis. Molecular background for thymol action is TRPV3 channel which is expressed on skin, tongue and afferent somatosensory neurons. We tested hypothesis that intranasal administration of thymol would modulate cough reflex in humans by trigeminal/olfactory pathways. 18 otherwise healthy volunteers, with normal ENT exams and normal lung function tests have been tested after nasal administration of thymol (0.025 ml,  $10^{-3}$ M) into both nostrils and urge-to-cough, cough threshold, cumulative and total count of coughs per provocation were estimated during standardized and validated capsaicin cough challenge. Nasal thymol challenges induced peasant olfactory sensations and in 6/18 subjects also mild cooling sensation, which was transient lasting up to 2 minutes, augmented with every inspiration taken during this interval. This is the first study which objectively documented the effect of nasal thymol drops on selected cough parameters in humans. Cough threshold was not influenced when comparing to intranasal saline and vehicle challenges (11.8 vs 12.7 vs 9.8 mM of capsaicin), but total count of coughs after nasal thymol challenge was significantly lower than that obtained after nasal saline or vehicle challenges (18.7 vs 20.3 vs 14.1 coughs/provocation;  $p < 0.05$ ). The most interesting and important finding was that subjects did not report urge to cough and urge to cough overlaps with C2 concentration, which is quite unique observation. Obtained data are similar to those we get after nasal menthol challenges. The question whether modulation of cough reflex by these herbal extracts (TRPM8 and TRPV3 agonists respectively) is of trigeminal or olfactory origin remains to be elucidated.

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