Streszczenie w j. angielskim

Smoking is one of the biggest threats to public health worldwide. Cigarette smoke contains more than 7,000 chemicals, including aldehydes, considered priority toxicants. A growing body of evidence supports the thesis of aldehydes as agents in the development of tobacco-related diseases.

β-escin (a mixture of triterpenoid saponins extracted from *Aesculus hippocastanum.* L.) is well known for its endothelial protection. In daily clinical practice, the main use of escin comes down to venotonic and venoprotective indications, where its anti-edema, anti-inflammatory and antioxidant properties are exploited. To date, literature data present the multidirectional effects of escin, confirming its safety profile, cytoprotective and therapeutic effects. However, recent advances in understanding its molecular mechanisms of action provide justification for new applications of β-escin. β-escin is a potent activator of aldehyde dehydrogenase (ALDH), an enzyme that catalyzes the oxidation of aldehydes to non-toxic carboxylic acids. β-escin may have potential applications in reducing negative health effects associated with smoking. The aim of this study was to evaluate *in vitro* and *in vivo* the effects of β-escin on biological processes in airways exposed to cigarette smoke.

The experimental study utilized nasal epithelial cells from non-smoking, healthy subjects, which were treated with β-escin (1μM) and CSE (5%) and then cell viability, ALDH activity and mRNA expression for ALDH isoforms were determined after 6 and 24 hours. 24-hour stimulation with β-escin increased the viability of nasal epithelial cells induced by CSE toxicity. Cell cultures exposed to CSE in the presence of escin showed a significant reduction in DNA damage. Both β-escin and CSE stimulated *ALDH3A1* expression (after 6 hours) and ALDH activity (after 24 hours), but the stimulatory effect was much stronger with simultaneous stimulation with β-escin and CSE. The presented results indicate a specific biphasic increase in mRNA expression of ALDH isoenzymes induced by CSE and β-escin. Both β-escin and tobacco smoke extract stimulated ALDH enzymatic activity, but the observed effect was much stronger when cells were simultaneously treated with CSE and β-escin. A similar phenomenon was found for mRNA expression for ALDH isoforms: simultaneous exposure of cells to β-escin and CSE led to the strongest increase in *ALDH1A1* and *ALDH3A1* expression after 6 hours, and after 24 hours for *ALDH1A3, ALDH3A2, ALDH3B1* and ALDH18A1. In addition, β-escin prevented CSE-induced inhibition of ALDH2 expression 24 hours after stimulation.

Application of β-escin solution in combination with chokeberry fruit extract for 7 days had an effect on the number of neutrophils in smokers' induced sputum. Smokers' sputum on day 0 contained a significantly higher number of neutrophils and fewer macrophages (%) compared to non-smokers. On day 7, the number of neutrophils in the smokers' sputum was significantly lower ($p=0.03$), reaching a level comparable to the control group. The applied treatment contributed to a reduction in IL-6 and IL-8 activity, but these changes did not reach statistical significance. The results of the pilot study suggest that low doses of β-escin combined with chokeberry fruit extract may exert a beneficial effect on tobacco smokers by significantly reducing neutrophil accumulation in the airways. A possible underlying mechanism may be due to the increased ALDH activity demonstrated in PBMCs both *in vitro* and *in vivo,* and the increase in antioxidant capacity found in both induced sputum and saliva.

We have shown, for the first time, that β-escin is an effective agent for supporting airway epithelial cells against cytotoxicity and DNA damage caused by cigarette smoke. It increases the antioxidant potential in airways exposed to a toxic agent such as cigarette smoke. The potential use of β-escin in protecting the respiratory tract from other cytotoxic agents such as air pollutants requires further study.