
SCREENING OF THE EFFECTS OF PLANT ALKALOIDS ON THE CONTRACTILE ACTIVITY OF RAT TRACHEAL SMOOTH MUSCLE CELLS

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Annotation

The article studies the effect of plant alkaloids 1-O-benzoylnapellin, zongorin, dihydroathysine and 6-benzoylheterathysine on the contractile activity of rat tracheal smooth muscle cells. It was found that 1-O-benzoylnapellin, dihydratizine, 6-benzoylheterazine and zongorin under conditions of KCl -induced contracture exhibit a relaxant effect, which may be due to their interaction with potential-dependent Ca²⁺ channels of plasma membranes and suppression of the entry of Ca²⁺ ions into the MMC of rat trachea.

Keywords: plant alkaloids, relaxant action, antispasmodic action, smooth muscle cells

Relevance

Bronchial asthma occupies a leading place in the structure of respiratory diseases, and its treatment remains one of the most important problems of modern pulmonology. According to a number of authors, the key link in the pathogenesis of bronchial asthma is increased tone and hyper reactivity of the smooth muscles of the airways [2,3,4].

The contractile activity of the smooth muscles of the airways is a dynamic process and varies depending on [Ca²⁺]_i [6, 14]. The enhancement of the contractile activity of smooth muscles is provided by Ca²⁺ ions coming from the extracellular medium through the potential-dependent and receptor-controlled Ca²⁺ channels of the plasma lemma [10, 13]. Considering the above, it is assumed that the increase in [Ca²⁺]_i observed in asthma and the associated increase in tone and hyperreactivity of smooth muscles occur as a result of impaired function of ion channels involved in the regulation of [Ca²⁺]_i in smooth muscle cells (MMC) [5,12,15]. In this regard, compounds capable of specifically modifying the function of the MMC ion channels have been considered in recent years as the most promising means for developing new approaches to correcting pathological conditions of smooth muscles [1,16].

Particular attention is paid to biologically active compounds produced by some plants, extracts of which have long been widely used in folk medicine for the treatment of bronchial asthma [7,8,9,11].

In this regard, as well as pursuing the goal of studying possible interaction plant alkaloids 1-O-benzoylnapellin and zongorin (isolated from a plant of the genus

Aconitum karakolicum Rapcs), and dihydroathysine and 6-benzoylheterazine (isolated from a plant of the genus Aconitum zeravschanicum Steinb) with Ca^{2+} channels of the L-type, we investigated their effect on the contractile responses of rat tracheal preparations induced by hyperkalium solutions.

Materials and Methods

The studies were carried out on isolated preparations of rat trachea under perfusion conditions with Krebs saline solution. Registration of the contractile activity of tracheal preparations was carried out using a mechanotron FT.03 (Grass., USA).

Discussion of the Results

According to the results of preliminary studies, these alkaloids under normal conditions in a wide range of concentrations do not themselves affect the tone of rat tracheal preparations. These data indicate that at rest these alkaloids do not act on functionally important structures of MMC and do not affect their contractile apparatus. However, in further experiments, we found that all the alkaloids studied were able to relax rat tracheal preparations previously shortened with hyperkalic solutions. This indicates that they have a relaxing or antispasmodic effect.

In particular, it was shown that under conditions of KCl-induced contracture, the most pronounced relaxant effect has 1-O-benzoylnapellin, in the presence of 200 microns of which the relaxation of the rat trachea preparation reached a maximum of $98,3 \pm 3,2\%$. At the same time, the EC_{50} value of the alkaloid concentration, at which it suppressed tracheal contractions by 50%, was 30 microns. Under similar conditions, 6-benzoylketerazine, dihydroathysine and zongorin also relaxed rat tracheal preparations with EC_{50} values of 35.3, 78.8 and 190 microns, respectively.

The results of these experiments indicate that 1-O-benzoylnapellin, dihydratizine, 6-benzoylheterazine and zongorin exhibit a relaxant effect under conditions of KCl-induced contracture, which may be due to their interaction with potential-dependent Ca^{2+} channels of plasma membranes and suppression of the entry of Ca^{2+} ions into the MMC of rat trachea.

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