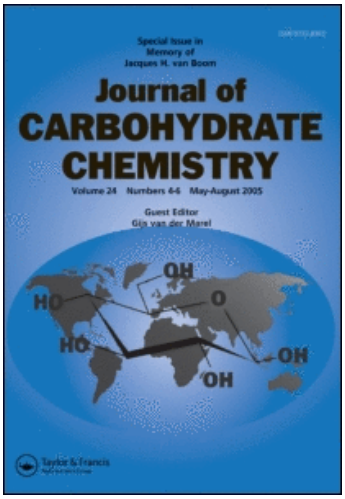

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ANTITUSSIVE ACTIVITY OF A RHAMNOGALACTURONAN ISOLATED FROM THE ROOTS OF *ALTHAEA OFFICINALIS L., VAR. ROBUSTA*

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ABSTRACT

Rhamnogalacturonan, one of the constituents of the mucilage isolated from the roots of marsh mallow, has been tested for antitussive activity on nonaesthetized cats of both sexes. The cough reflex was induced mechanically. It was found that rhamnogalacturonan reduced significantly the number of cough efforts and the intensity of attacks from the irritated laryngopharyngeal and tracheobronchial mucose membranes of the airways and promoted expectoration. The exhibited activity was found to be lower than that of the narcotic codeine, but higher than those of the comparative nonnarcotic drugs.

INTRODUCTION

Phytotherapy has at its disposal a wide range of biologically active compounds, the structures and specific activities of which are not in all cases fully understood. Mucilages, constituted from appreciable proportions of polysaccharides and protein-polysaccharide complexes, occupy a significant place in this group of compounds. They are used not only for binding of various preparations or as bulking agents for low amounts of ingredients, but also as direct drugs.

It is known[2] that coughing is one of the main symptoms of airways' illness. When coughing ceases to fulfil its physiological function, it becomes a pathological reflex burdening the organism of the patient. Then it is necessary to suppress or at least keep this reflex at a reasonable level. As the medicinal plant marsh mallow *(Althaea officinalis L.)* has long been known for its curing effects in treatments of catarrhs of the respiratory system and various inflammations of oral and nasal cavities, in our previous work[3] we tested for antitussive activity from both the complex water extract and the mucilage isolated from the roots of this plant. The results were promising. The musilage, a mixture of mainly glucans,[4] arabinan,[5] and an acid heteropolysaccharide,[6] was able to suppress the cough reflex more expressively than the complex water extrat and comparably to some preparations generally used in clinical practice. This recognition prompted us to undertake further experiments in order to find out the extent of contribution of the individual polysaccharide components of known primary structures to the total activity of the mucilage.

The present communication provides results on tests for antitussive activity with the acid heteropolysaccharide, which seemed to be the most interesting component of the mucilage due to its uronic acid content with active carboxyl groups.

RESULTS AND DISCUSSION

Rhamnogalacturonan, an acid heteropolysaccharide component of the mucilage isolated from the roots of marsh mallow, was tested for antitussive activity on cats of both sexes. According to Korpáš an Nosáľová,[7] cats are the most suitable animals for cough modeling and testing of various preparations for their effect on the cough reflex. The cats were nonanaesthetized in order to eliminate the possibility of influencing the results by the anaesthetics. The cough reflex was induced by mechanical stimulation of laryngopharyngeal and tracheobronchial mucose areas of the airways. We preferred mechanical to chemical or electrical stimulation because this impulse simulates in the most

suitable way the natural conditions when cough is induced by foreign solids. Moreover, it is point stimulation, the intensity of irritation is constant, and the possibility of adaptation of receptors to this kind of irritation is unlikely.[8]

Peroral administration of rhamnogalacturonan in a dose of 50 mg/kg b.w. brought about a statistically significant decrease of number of efforts and intensity of cough attacks in expirium and inspirium both from the laryngopharyngeal and tracheobronchial regions (Fig. 1). The cough frequency from both areas was reduced significantly, too, while the intensity of maximum cough efforts, particularly from the tracheobronchial area, was not suppressed significantly (Fig. 2). The cough parameters were found to be suppressed significantly within 30 min after administration of the compound and the decrease lasted during the whole period (5 h) of observation. When the drug had not been administered to the animals and the airways were irritated at the respective time intervals, the cough parameters showed no significant changes. Undesirable side effects were not observed after administration of the rhamnogalacturonan.

In order to recognize the importance of the observed antitussive activity of this polysaccharide, we performed comparative experiments with some drugs generally used in clinical practice, i.e., dropropizine, prenoxdiazine, Sirupus Althaea, and codeine. These drugs were tested for their ability to suppress the cough parameters most important from the clinical point of view, namely the number of efforts and the intensity of cough attacks in expirium and inspirium. Moreover, we reproduced the tests already accomplished[3] with a new sample of the mucilage (50 mg/kg b.w.) wherefrom the rhamnogalacturonan was obtained so that the results for comparison would be more authentic. The results obtained are illustrated in Fig. 3 together with the activity values of rhamnogalacturonan. It is evident from this figure that the activity of rhamnogalacturonan (50 %) was lower than that of the most frequently used narcotic codeine (62 %), but higher than those of the nonnarcotic drugs. The significance of this polysaccharide becomes pronounced also in comparison to the mucilage. The twice higher activity in this relation suggests

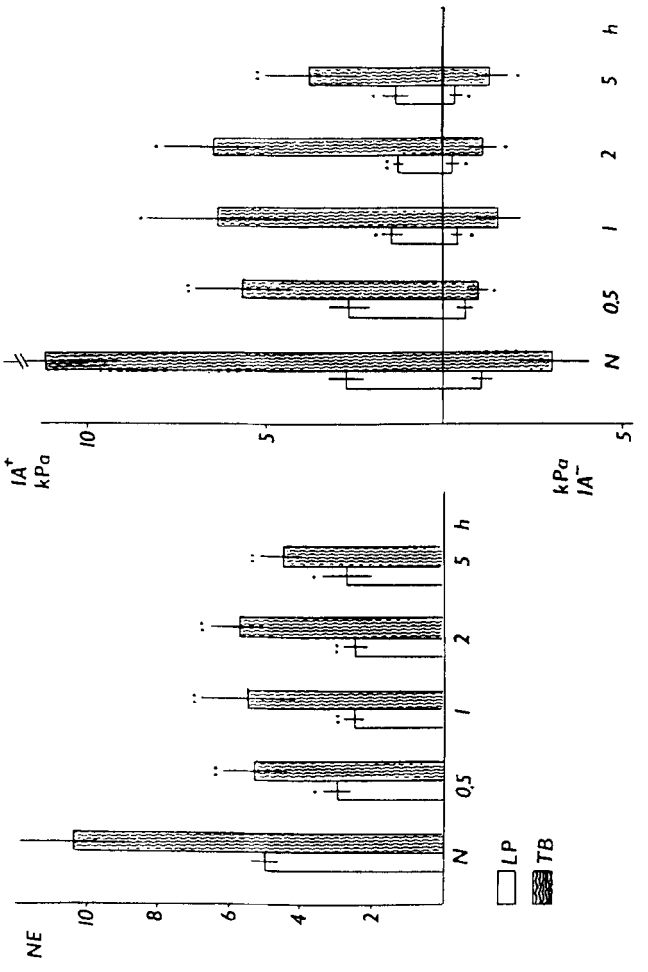

FIG. 1. Effect of rhamnogalacturonan (R; 50 mg/kg b.w.) on number of efforts (NE) and intensity of cough attacks in expirium (IA^+) and inspirium (IA^-) from the laryngopharyngeal (LP) and tracheobronchial (TB) areas. N = normal values of cough parameters; the column represents the mean values of cough parameters; the range denotes standard error of means; 5 % significance is marked with one dot, 1 % with 2 dots.

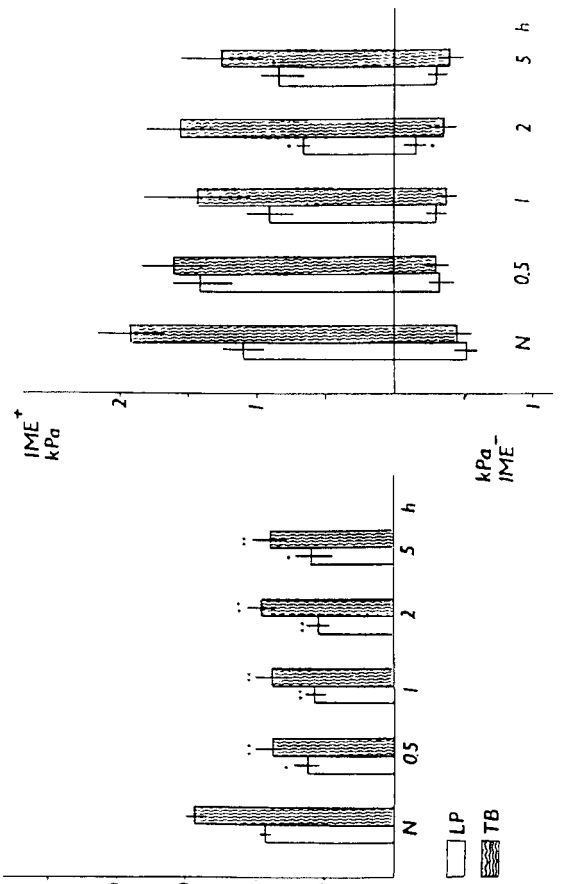

FIG. 2. Changes of cough frequency (NE min^{-1}) and intensity of maximum expiratory (IME^+) and inspiratory (IME^-) cough efforts after administration of the rhamnogalacturonan.

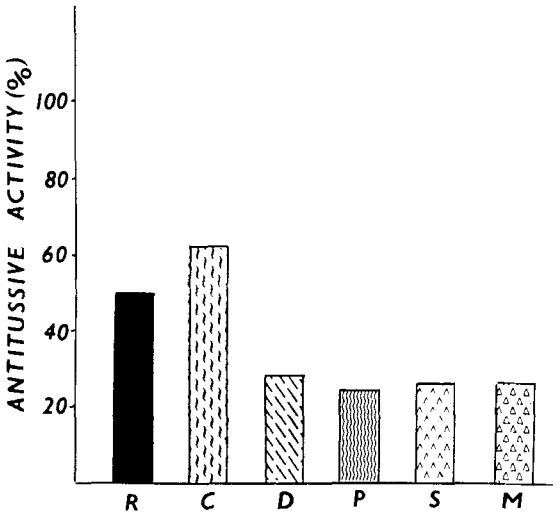

FIG. 3. Effect of rhamnogalacturonan on cough parameters (NE + IA) in comparison to those of commercial drugs. R = Rhamnogalacturonan; C = Codeine; D = Dropropizine; P = Prenoxdiazine; S = Sirupus Althaea; M = Mucilage.

a relatively high contribution to antitussive activity of the mucilage, when considering the fact that rhamnogalacturonan represents only about 20 % of the total composition of the mucilage.

In conclusion, it may be stated that rhamnogalacturonan caused a noticeable decrease of all cough parameters followed, except for the intensity of maximum cough efforts. This finding is considered significant from a clinical point of view because it indicates that the tested compound suppressed the cough reflex but promoted expectoration.[9] With regard to the above mentioned results and to the fact that rhamnogalacturonan surpassed the effect of the nonnarcotic drugs approved experimentally and clinically,[7] this polysaccharide may be considered a potential cough reflex-suppressing agent, which could be partly substituted for some synthetic drugs. Furthermore, undesirable side effects were not observed in the experiments. The fact that the antitussive effect was observed in a relatively short time after administration of the polysaccharide, and lasted during the whole period of the experiment, might be utilized

in clinical practice when establishing the administration scheme of the drug.

Our next work will be concerned with antitussive activity tests on the dominant neutral polysaccharide component of the mucilage.

EXPERIMENTAL

Rhamnogalacturonan (R) was obtained in our laboratory by separation from the mucilage (M) isolated from the roots of marsh mallow.[6] Sirupus Althaea (S), the nonnarcotic prenoxdiazine (P) and dropropizine (D), and the narcotic codeinium dihydrogen phosphoricum (C), used for comparative tests, were commercial products generally used in clinical practice. All compounds tested were administered perorally in the form of a water solution. The doses of the individual comparative drugs used herein, i.e., S = 1000 mg/kg b.w., P = 30 mg/kg b.w., D = 100 mg/kg b.w., and C = 10 mg/kg b.w., represented the amounts which in the earlier experiments exhibited the highest antitussive effects. Changes of cough parameters were recorded with a Biograph 12-03 electromanometer. The results of experiments were evaluated by the method of Wilcoxon and Wilcox.[10]

Nonanaesthetized cats of both sexes weighing 2000 - 3000 g were used for the experiments (10 in each set). Chronic tracheal cannula were placed into the animals according to the method described by Korpáš *et. al.*[11] The cannula enabled mechanical stimulation of the airways and, at the same time, served for recording of the changes in the side tracheal pressure. Cough was induced with a nylon fibre of 0.35 mm diameter. The mucous membrane of the laryngopharyngeal (LP) and tracheobronchial (TB) areas of the airways was stimulated consecutively five times. Of cough parameters evaluated were the number of efforts (NE), intensity of cough attacks in expirium (IA^+), and inspirium (IA^-), cough frequency (NE min^{-1}), and intensity of maximum cough efforts in expirium (IME^+) and inspirium (IME^-). The values of these parameters obtained before administration of the preparations represented the normal values (N). The effect of drugs was followed after administration in time intervals of 0.5, 1, 2 and 5 h.

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