

EFFICACY OF PROSPAN APPLICATION IN CHILDREN'S DISEASES OF RESPIRATORY TRACT

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At present time, diseases of respiratory tract are the major problem in children's morbidity. These are also the third cause of children's mortality from perinatal pathology and congenital anomalies. This is why the respiratory pathology was always in the center of attention of pediatricians – and still is.

It is well known at the moment that pathogenesis of respiratory diseases generally causes intensive production of bronchial mucus, obstruction of the upper airways and cough [1]. Therefore the treatment of inflammatory diseases of the respiratory tract mostly is a symptomatic therapy which includes mucolytic agents, expectorants and bronchodilators.

There are a lot of expectorants available at the modern days. One of the herbal expectorants is Prospan® [2]. The drug contains glycosilated terpenesaponins, phytosterols, polyynes, essential [volatile] oil, flavonoids, which all cause an expectorative action (mucolytic, secretolytic and mucokinetic) as well as bronchospasmolytic, antimicrobial and anti-inflammatory effects [3-7]. Prospan® reduces the viscosity of the mucus and eases its expectoration [5,6]. Drug is produced in form of syrup or effervescent tablets, which both have a palatable taste, and contain as active ingredient the extract of dried ivy leaves (drug extract ratio 5-7,5:1) [2]. Prospan® in the dosage form as syrup can be used to treat infant babies. Besides that, the syrup contains sorbitol as sweetener, so it is safe for children with pancreatic [insular] diabetes too. It does not cause any surplus of carbohydrates.

The aim of this study was to document the efficacy and tolerability of Prospan® syrup in the treatment of children suffering from acute inflammatory diseases of the respiratory tract.

Materials and methods.

72 children aged from 7 months to 15 years were treated under inpatient care, 42 in Kiev clinical hospital #6 and 30 in Dnepropetrovsk state clinical hospital #5. Excluded from the study were patients with the following diagnoses: fructose intolerance; severe heart, kidney and liver diseases; known or expected hypersensitivity to the tested drug as well as those patients taking other medicine which influences respiratory diseases (e.g. other expectorants) and also patients that were included in other studies within the last 3 months.

All patients were documented by using the clinicodiagnostic laboratory during the process of treatment. The documented parameters were clinical symptoms (such as duration of fever, cough, ease of expectoration, character of breathlessness, auscultatory picture of patient's lungs) and blood analyses, including the calculation of leukocytic count, flora identification, virological and bacteriological tests. The functioning of external respiration was explored with Master Lab diagnostic complex provided by Erich Jaeger (Germany), and also peakflowmetric and respirosonographic data were evaluated.

The documentation of subjective symptoms was done within a patient's diary. Children or their parents filled in their own impressions from the treatment process. Efficacy of treatment was rated by using a 5-score rating scale. Both clinical results and subjective impressions were taken into consideration for the evaluation of efficacy. Besides that, it was documented when the drug exerted the first effect. Additionally the taste of the product was subject of evaluation.

Patient allocation by clinical diagnosis is shown in table 1. Concomitant diseases were documented for some patients: compensated tonsillitis (n=18), biliary dyskinesia (n=6) and vegetative-vascular dysfunction (n=6).

Table1: Clinical diagnoses of documented patients

Diagnosis	Number of patients (n)	Number of patients (%)
Acute respiratory viral infection (ARVI)	6	8,3
Acute bronchopneumonia	19	26,4
Acute (simple) bronchitis	25	34,7
Acute obstructive bronchitis	11	15,3
Recurrent bronchitis	4	5,6
Bronchial asthma	5	6,9
Mucoviscidosis	2	2,8
Total	72	100

Out of 20 virologically and microbiologically inspected children, 5 suffered from viral infection (parainfluenza virus 2, respiratory-deciduocellular virus 3), and in 6 cases autoflora was detected (2 with epidermal staphylococcus, 1 with pneumococcus, 3 with streptococcus). In 1 child mycoplasma and in 2 children a microbial mixture (epidermal staphylococcus and respiratory-deciduocellular virus, streptococcus + parainfluenza virus) could be observed. When required children were treated with antibiotics, predominantly cephalosporins.

For symptomatic treatment most patients (53 children) were treated with Prospan[®] syrup. Prospan[®] was prescribed for monomucolytic therapy in the following dosages: from 1 to 6 years old - 1 teaspoonful 3 times a day; from 7 to 14 years old - 2 teaspoonsful 3 times a day. Treatment duration was depending on the character and severity of the disease. In case of acute pathology the treatment lasted 7-10 days, in case of chronic disease

treatment duration was 10–14 days. In 72% of the patients Prospan[®] was given 3 days after the beginning of the disease, in 19% after 4 days and in 9% of patients after more than 4 days. The start of treatment generally was depending on the time of hospitalization (when children started to be under inpatient care).

In the study also patients treated with Ambroxol syrup were documented (19 children). The baseline inflammatory process severity and the main clinical manifestations were equal for both groups.

Results and their discussion.

In the clinical picture of acute respiratory tract infection the children suffered predominantly from the following symptoms: cough (97,5%), rhinorrhoea (54,5%) or blocked nose (84,6%); in 74.4% auscultation anomalies could be detected. Short breath (34,2%), auscultation of lungs with dry (38,6%) and / or moist (42,4%) crepitation, crepitation (28,4%) as well as prolonged inhalation (21,8%) were diagnosed in those patients with acute bronchopneumonia, bronchial asthma and mucoviscidosis.

According to the study protocol the patient condition was documented once a day. Evaluation of clinical efficacy was done at day 3, day 7 and day 14 of treatment according to a 4-point scale as: excellent, good, poor, no effect.

The results of the clinical evaluation of Prospan[®] efficacy are shown in fig.1 (assessed by doctors and by the children or their parents).

In 90,1% the efficacy was rated by the doctors as excellent or good. This rating was similar to that done by the patients or parents, respectively - excellent and good in 87,1% of all cases. No effect was displayed in 3,3% of cases each.

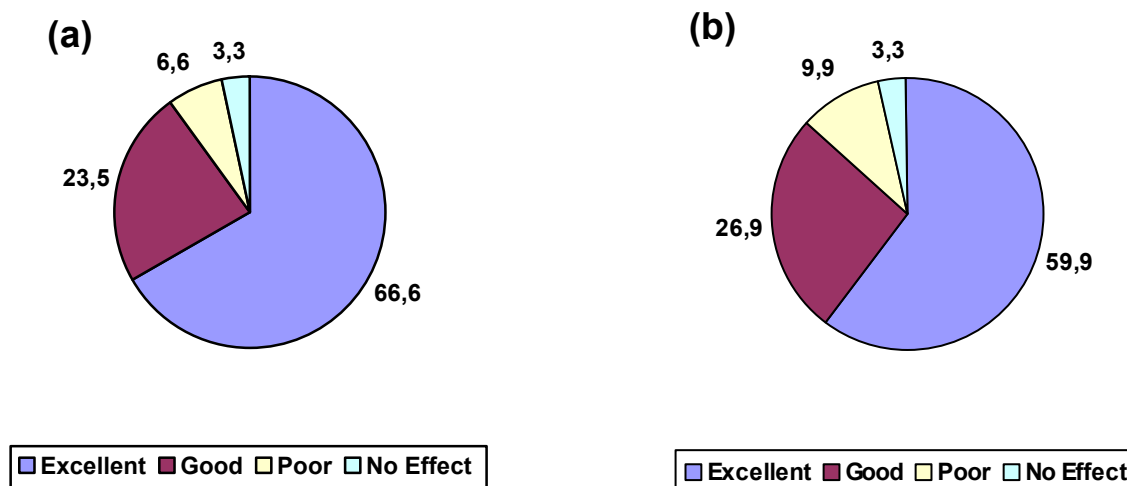


Fig. 1. Clinical evaluation of efficacy of Prospan[®] (by doctors (a) and children / parents (b)).

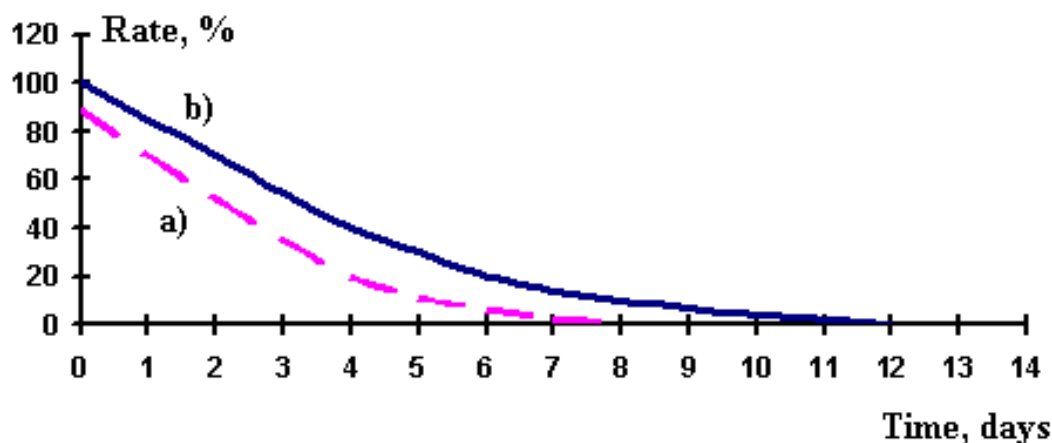


Fig.2. Cough duration course during Prospan[®] therapy (according to doctors' observation)

Along with the evaluation of clinical efficacy, the objective symptoms were taken into consideration as well. The cough character and duration was one of them. The course is shown in Fig.2.

The course of the auscultatory picture of lungs during Prospan[®] treatment is shown in Fig.3. Among the children with respiratory tract infection, the cough became productive 3-4 days after Prospan treatment started, and within 7-8 days after beginning the treatment it was gone completely.

In the group of children with bronchitis (depending on the character of the disease), the positive effect was seen about 2-3 days later

compared to the group of patients suffering from respiratory tract infection.

Physical changes in lungs and difficult breathing was seen in general during the first 6-7 days of therapy, but prolonged inhalation disappeared at the 5th day of treatment. Practically at the same day the dry & moist crepitations in lungs were gone as well (Fig. 4).

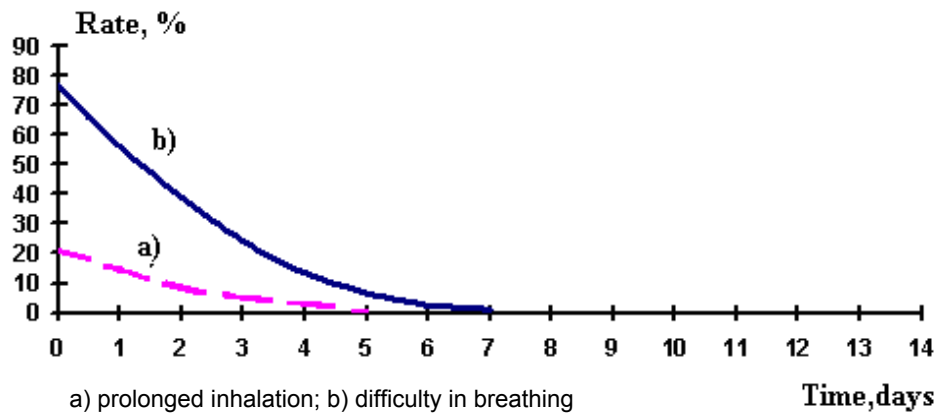


Fig. 3. The course of auscultatory picture in lungs during Prospan® therapy

In children with acute obstructive bronchitis, bronchopneumonia, recurrent bronchitis or exacerbation of bronchial asthma, the external respiration was documented during Prospan® treatment by spirometry measurements (see table 2). External respiration parameters (such as exhalation volume, maximum available speed of expiratory air flow; maximum inhalation weight hour space velocity within 25% of lungs vital volume; maximum inhalation weight hour space velocity within 50% of lungs vital volume and Tiffno index were normalized within 6-7 days after treatment was started in the group of children with acute obstructive bronchitis.

For children suffering from bronchopneumonia and exacerbation of bronchial asthma the external respiration parameters were normalized in general within 9-11 days after the beginning of treatment. However, in case of bronchial asthma the external respiration velocity was below normal even after treatment, which gives a hint to high-grade abnormalities of airway functioning in this group of patients (see table 2).

Due to the fact that the external respiration weight space velocity normalized during the treatment within the group of patients with obstructive abnormalities we can summarize that Prospan® has a high-grade broncholytic action.

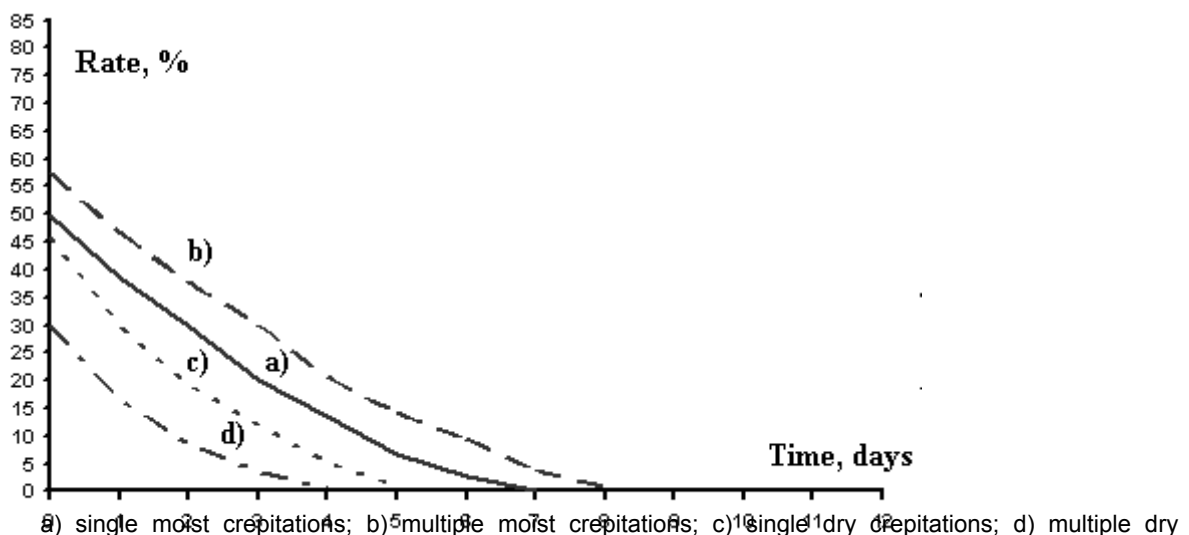


Fig. 4. The course of auscultatory picture in lungs during the Prospan® treatment

Normalization of leukocytic count was documented after 7 ± 1.5 days for all patients. SOE parameter was normalized in 12 ± 2.4 days.

Respective to the positive course of clinical and functional parameters during the treatment with Prospan®, it was most interest to have a look at the

results within the group of children treated with Ambroxol. The course of main clinical symptoms is shown in graphics. In particular, the course of short breath in both treatment groups is shown in Fig. 5. As it is to see, short breath disappeared completely after 3 days of treatment. At the same time the rate of patients with short breath increased a little bit at the

3rd day of treatment, especially in the Ambroxol group. Probably the used drugs stimulate primarily the formation of mucus but do not provide its proper evacuation, what brings up an increase of short breath. Most intensively it was displayed during the Ambroxol treatment.

Table 2: The course of external respiration (in % of normal) during Prospan® treatment

Index	Before treatment				After treatment			
	Acute obstructive bronchitis	Recurrent bronchitis	Broncho pneumonia	Bronchial asthma	Acute obstructive bronchitis	Recurrent bronchitis	Broncho pneumonia	Bronchial asthma
VC, %	89,3±2,7	95,3±2,4	74,3±3,1	93,1±3,7	92,3±3,0	96,2±2,2	88,2±2,7	97,3±3,2
FVC, %	94,2±2,1	97,1±2,5	75,8±6,3	91,2±2,6	95,3±2,7	98,2±2,5	87,8±3,5	96,8±3,1
FEV ₁ , %	79,5±3,2	89,8±3,8	77,6±4,1	73,6±5,2	86,2±2,5	93,2±2,1	85,6±4,2	84,3±3,2
PEF, %	65,4±3,7	87,2±4,1	75,7±5,3	70,1±2,7	83,8±3,1	91,4±2,3	83,5±3,8	77,5±3,6
MEF ₂₅ , %	59,4±4,3	85,7±4,0	68,9±5,6	54,2±7,1	77,0±3,4	90,2±2,1	77,4±3,2	68,4±4,8
MEF ₅₀ , %	52,3±4,7	83,3±4,8	64,3±6,1	47,4±9,3	72,4±2,3	90,7±2,8	75,3±4,3	66,3±3,9
Tiffno index, %	64,3±1,5	69,3±2,4	65,5±1,5	63,8±1,7	87,9±1,6	81,0±1,8	77,4±2,5	71,5±3,8

Notes: VC – vital lung volume; FVC - forced vital lung volume; FEV₁ – forced exhalation volume within first second; PEF - maximum expiration weight hour space velocity of air flow; MEF₂₅ - maximum inhalation weight hour space velocity within 25% of lung vital volume; MEF₅₀ - maximum inhalation weight hour space velocity within 50% of lung vital volume.

The comparison of the decrease in productive cough in both treatment groups showed no statistically significant differences (see Fig. 6). After 7

days of treatment the cough in both groups was healed in more than half of the patients, and within 14 days it disappeared in general.

Fig. 5. Course of short breath in Prospan® and Ambroxol treatment groups

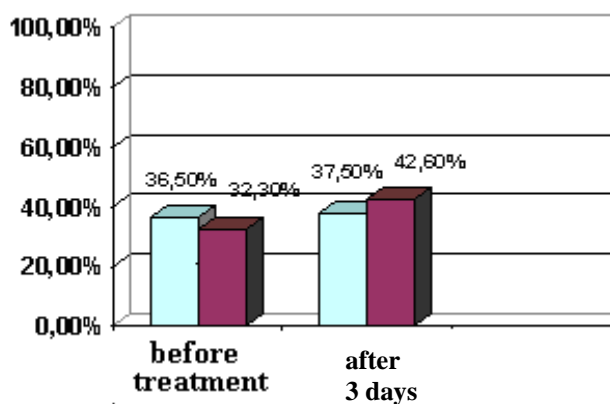
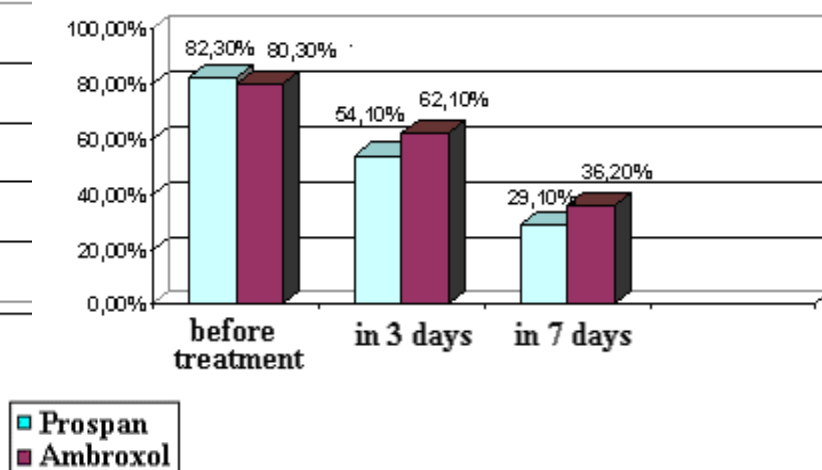


Fig. 6. Productive cough in Prospan® and Ambroxol treatment groups



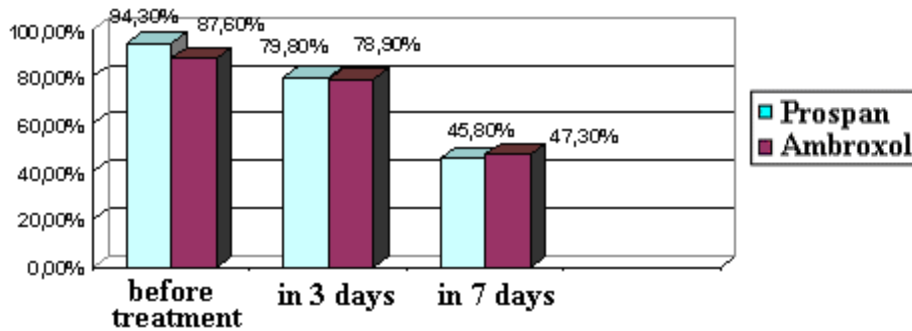


Fig. 7. Course of auscultatory picture in lungs in Prospan® and Ambroxol treatment groups

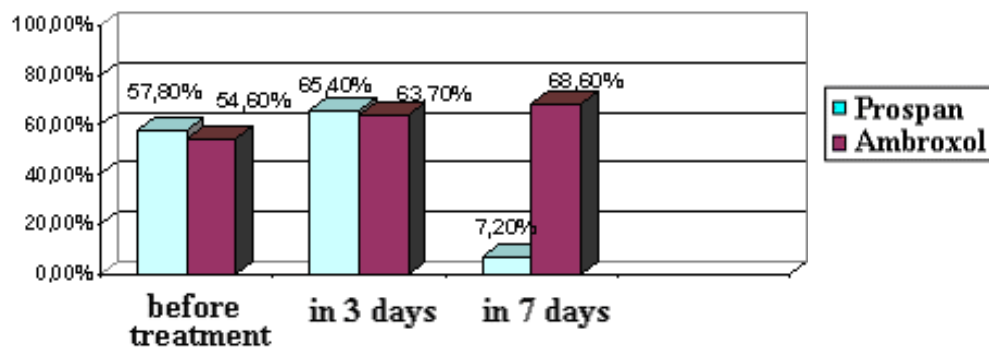


Fig. 8. Normalization of external respiratory velocity parameters in the Prospan® and Ambroxol treatment groups.

Comparing the course of auscultatory picture in lungs in both Prospan® and Ambroxol treatment groups, the fast decrease of crepitation was seen only in the group of children treated with Prospan® (see Fig. 7).

Quite interesting were the results respective to the normalization of velocity parameters in the Prospan® and Ambroxol treatment groups (see Fig. 8). It can be seen that after 7 days of Prospan® treatment the velocity parameters of external respiration were normalized nearly in all children with obstructive diseases, while in the Ambroxol treatment group a normalization could not be documented, but the parameters even got worse. Therefore, with respect to velocity parameters Prospan® causes much greater improvements than Ambroxol. Apparently, the positive effect of Prospan® is due to the broncholytic action of the drug.

It is also necessary to notify along with the good treatment efficacy of Prospan® that this product is much more handy in patient's use, especially when applied to children of preschool and primary school

age (Prospan® syrup has a palatable taste), and it also does not bear the risk of adverse reactions.

Studies to evaluate the efficacy of Prospan® revealed high efficacy and safety of this remedy for the treatment of children with respiratory tract pathologies. Besides, high-rate positive effects could be observed even when applied to babies younger than 1 year old. Drug prescription in a therapeutic dose brings to high-grade clinical course of disease symptoms, which come up as short breath reduction, cough reduction and improvement of auscultatory picture. The normalization of external respiratory velocity parameters as well as data of peakflow measurements permits the prescription of this drug for children with obstruction in the upper airways.

In that way, the high-effective mucolytic and broncholytic action of Prospan® allows to recommend this drug for a complex treatment of respiratory tract pathologies to children of all age groups.

References

1. V.Maidannik. Clinical recommendations on diagnosing, treatment and prophylaxis of children's upper airway diseases. – Kiev, "Aspect Polygraph", 2003. – 177 p.
2. V.Maidannik, M.Schupak, O.Kachalova. Prospan and its abilities in clinical pediatrics. // Pediatrics, tocology and gynaecology. – 2003. – № 1. – p. 33–38.
3. Breitkeuz J., Kleinebudde P., Boos J. Kindgerechte Arzneiformen – Arzneimitteltherapie für alle.- Pharm.Ztg.147 Jhg., 2002.-P16-24
4. Hecker M., Runkel F., Völp A. Treatment of chronic bronchitis with ivy leaf special extract – multicentre post marketing surveillance study with 1350 patients. Forschende Komplementärmedizin und Klassische Naturheilkunde, 9, 2002.-P.77-84.
5. Mansfeld H.-J., Höhre H., Repges R., Dethlefsen U. Sekretolyse und Bronchospasmodolyse – Klinische Studie: Behandlung von Kindern mit chronisch obstruktiven Atemwegserkrankungen. TW Padiatrie 10. 1997.-Nr.3.-P.155-157.
6. Mansfeld H.-J., Höhre H., Repges R., Dethlefsen U. Therapie des Asthma bronchiale mit Efeublätter-trockenextrakt. MMW 140., 1998.-Nr.3.-P.26-30.
7. Meyer-Wegener, J., Liebscher K., Hettich M. Efeu versus Ambroxol bei chronischer Bronchitis. ZFA 69., 1993.-Nr.9.-P.61-66.

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