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EFFECTS OF SEAPROSE ON THE RHEOLOGY OF BRONCHIAL MUCUS IN PATIENTS WITH CHRONIC BRONCHITIS. A DOUBLE-BLIND STUDY VS PLACEBO

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*Summary: There are changes in the rheological characteristics of mucus (viscoelasticity) in several pulmonary pathologies, and especially in chronic bronchitis. Seaprose, a proteolytic enzyme, is one of the pharmacological possibilities for affecting the rheology of bronchial mucus to correct mucostasis and improve its clearance. The action of this drug on the viscoelasticity of bronchial mucus was assessed in a double-blind vs placebo study with 20 randomly balanced chronic bronchitis patients using a new kind of portable rheometer with special features designed for routine bronchial mucus analysis in clinical practice at the patient's bedside. It was found that in the group of patients who were given the placebo, there were no particular changes in the rheological behaviour of mucus, while in those patients who were given seaprose there were significant changes in both viscosity and elasticity at the end of treatment. Eight days after the end of treatment with seaprose, there was still a significant beneficial effect on the viscoelasticity of mucus and a sort of "post-mucolytic effect" can be postulated. Seaprose also had antiinflammatory action, and since in chronic bronchitis there are variable degrees of inflammations, its beneficial long-lasting effect could also be ascribed to this concomitant action.*

#### Introduction

The production of bronchial mucus and mucociliary clearance are important defence mechanisms of the respiratory airways against noxae of various origins. When such noxae cause a defensive reaction that increases the production of mucus and an alteration in its rheological properties, the normal mucociliary transport becomes impaired and a partial reduction in ventilation can occur;

moreover, because of the mucostasis involved, bacterial colonization is also favoured.

Changes in the rheological characteristics (viscoelasticity) of mucus and in the reciprocal relationships among mucus, cilia and periciliary fluid are "common denominators" in several pathological conditions such as acute and chronic bronchitis, cystic fibrosis, bronchiectasis and asthma

The primary clinical therapeutic goal in any disease is to remove the offending cause. This obvious goal is often not easy to achieve in clinical broncho-pneumological practice, and there are mucostasis must be corrected with drugs that act on mucus

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were carried out within 10 min after it was obtained. At this time, the body temperature of the patients never exceeded 37°C, room temperature was between 20 and 25°C and humidity between 51 and 77% at the time of sputum collection and during the following examinations. The rheological behaviour of bronchial secretions was studied with a rheometer supplemented by innovative features aimed at routine bronchial mucus investigation at the patient's bedside to simplify and automate the measuring procedure (13). A Searle-type configuration with a coaxial cylinder sensor system and the Mooney-Ewart geometry were adopted. Dynamic viscoelasticity was measured by stepwise increasing of the torsional oscillation of the bob to the sample with a shearing stress  $M(t)$ , which is known *a priori*, because it is generated by a magnetic torque-motor driven electronically through a specific software programme by a micro-processor. The torsion generated is proportional to the square of the current applied (range of oscillation: 0.02–0.5 Hz). Simultaneously, the shear strain and the shear rate were recorded from the angular movement (optical encoder HP 4000 with a resolution of 0.00157 rad) (13) and the angular velocity. After these measurements had been collected, a second software programme was used to calculate in real time the correlations among the different parameters recorded, to give the viscoelastic measurement.

The results were printed automatically on paper, together with a Lissajous figure whose shape is related to the viscoelastic features of the sample, by an  $\alpha$ -numerical printer located at the top of the instrument. The whole procedure takes 3–5 min, depending on the characteristics of the sample. In one hour, therefore, about twelve samples can be investigated.

The innovative feature of a disposable bob and cup (sample volume = 0.75 ml) is very useful because it not only makes the procedure more rapid, but also safeguards the operator from contact with the sputum, with protection against pathogens

such as bacteria, virus, AIDS, hepatitis (13)

The viscoelastic measurements were made on days –3 and 0 to check that these two values did not differ by more than 20%, as a precaution to avoid patients with irregular behaviour. Measurements were repeated after 10 days, at the end of treatments, and then at 14 and 18 days, to follow the post-mucolytic behaviour. The criterion for inclusion in the study was a viscosity on days –3 and 0 not lower than 3,000 mPas and not higher than 20,000 mPas. Results were evaluated by Student's *t* test for paired data and by ANOVA

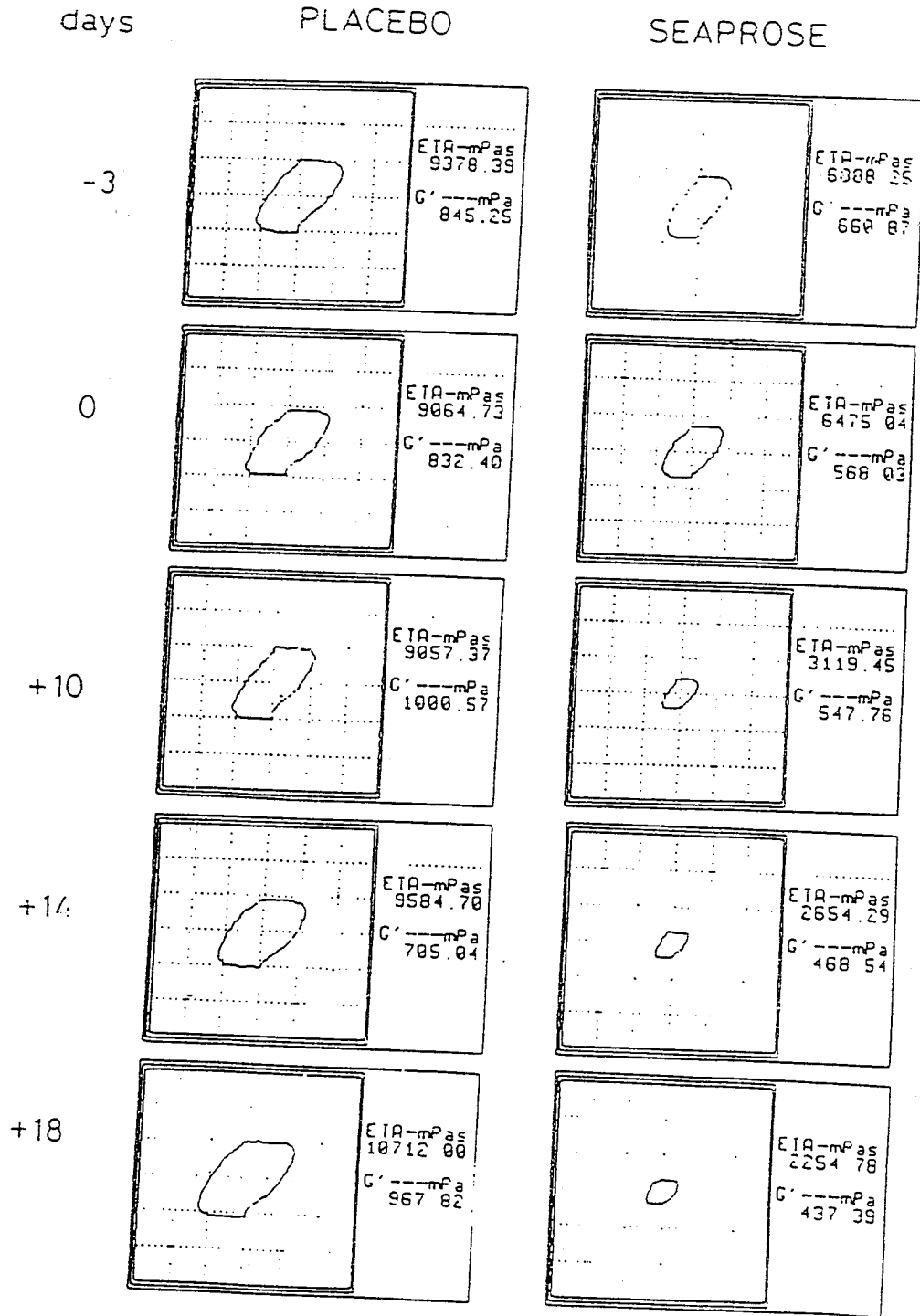
## Results

At the end of the study the envelopes with the keys to identify the treatments of patients were opened and the values of viscosity for those treated with placebo or with seaprose were grouped in Table I. The corresponding findings for elasticity were grouped in Table II. In the group of patients given placebo, there were no statistically significant differences between before and after treatment. In the group given seaprose, there were significant differences in the mean values of viscosity and elasticity. An example of the sequences of the corresponding Lissajous values is shown in Fig. 1.

Table III shows the mean values for the different respiratory parameters investigated, e.g. V.C., FEV<sub>1</sub>, Tiffeneau index, Motley index, TPC, and RV and for the different days. No significant differences were found in either group of patients between and after treatment. Blood analyses also did not reveal any particular changes attributable to the treatments

## Discussion

In chronic diseases every patient has his own cycle of evolution and chronic bronchopneumopathies have their own cyclic courses as well.



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