The Effects of Mucolytic Agents and Stirring on Sputum Viscoelasticity

TAMOTSU TAKISHIMA, SHIGERU SATO, TAKESHI AOKI and SHINSAKU MAEDA

The First Department of Internal Medicine, Tohoku University School of Medicine, Sendai, 980

TAKISHIMA, T., SATO, S., AOKI, T. and MAEDA, S. The Effects of Mucolytic Agents and Stirring on Sputum Viscoelasticity. Tohoku J. exp. Med., 1980, 131 (2), 103-117 — Changes in the behavior of sputum viscoelasticity due to differences in macroscopic appearance of sputum brought about by stirring and those due to the addition of an expectorant to purulent sputum in vitro, were studied in a coaxial cylinder rheometer. First, initial results from stirring the sputum indicated the following: Samples of untreated sputum showed no obvious differences among the three macroscopic groups, mucoid, mucopurulent and purulent, on the basis of dynamic viscoelasticity. However, when they were stirred sufficiently, dynamic viscosity and storage modulus increased in mucoid sputum and decreased in purulent sputum. Second, the addition of expectorants revealed the following results: (i) When distilled water was used as a control substance added to sputum, the addition of 0.5% semialkaline proteinase to sputum decreased the dynamic viscosity and storage modulus of the sputum to a large extent. (ii) The addition of 0.2% Bromhexine exerted a small influence upon the dynamic viscosity and slightly increased the storage modulus. (iii) The addition of 20% N-acetyl-L-cysteine increased the dynamic viscosity slightly, but decreased the storage modulus to a large extent. In brief, each expectorant exerted a unique influence on the viscoelasticity of sputum. These results were discussed with regard to their clinical significance. — sputum viscoelasticity; stirring; mucolytic agent

In patients with pulmonary disease, an excessive production of sputum and failure of its expectoration from the airways can be causes for the occurrence of severe respiratory insufficiency. To establish an effective treatment of these cases, it is essential to understand correctly the dynamic behaviors of sputum in the bronchial lumen and the patho-physiology of expectoration. To understand objectively how readily tracheo-bronchial secretions can be expectorated, at least two mechanisms of expectoration must be elucidated: (i) the dynamic behavior of sputum at the time of coughing, and (ii) the behavior of secretions in the bronchial lumen induced by the movement of cilia. This process is thought to be heavily influenced by the rheological properties. Although some investigators have compared the macroscopic appearance of sputum with its rheological properties, considerable discrepancies have been reported (Bruce and Quinton 1962; Nicholas 1964; Lieberman 1968; Denton et al. 1968; Feather and Russell 1970; Palmer et al.

Received for publication, May 18, 1979.
1970; Dulfano et al. 1971; Sturgess et al. 1971; Charman and Reid 1972; Mitchell-Heggs et al. 1974; Picot et al. 1978). Furthermore, little is known about the effects of stirring, a common treatment before testing, on the viscoelasticity of sputum irrespective of macroscopic variety (Baldry and Josse 1968; Reid 1973).

On the other hand, various expectorants are usually administered to patients suffering from pulmonary disease. Although the mechanism of action is not the same for all of them, it is supposed that every expectorant eventually modifies the dynamic behavior of secretions in the bronchial lumen when administered to patients, thereby displaying an effect. Accordingly, it is of great interest from a rheological point of view to clarify what parameter of the rheological behavior of sputum has been modified by an expectorant and consequently how the behavior of secretions in the bronchial lumen has been influenced by this modification. Khan et al. (1976) reported effects of mucolytic agents on the rheological properties of tracheal mucus obtained from dogs; however, the effect on the viscoelasticity of sputum obtained from patients is not always defined.

The purpose of the present study was to investigate changes in the viscoelastic behavior of sputum due to differences in macroscopic appearance brought about by stirring, and those due to the addition of an expectorant to purulent sputum in vitro.

**Materials and Methods**

A coaxial cylinder rheometer developed by Umeya et al. (1974) (hereafter referred to as a thixotrometer) was used for the experiments. The thixotrometer used is outlined in Fig. 1. It is composed of four portions: (A) a cylinder system, (B) a power source, consisting of a servo-motor and a gear transmission, (C) a heat regulator, and (D) a torque recorder. A sample of fluid to be measured is placed in the space between the concentric inner and outer cylinders. By the aid of the component for speed transmission to which a servo-mechanism has been applied, a torsional oscillation or rotation is selected from a range of varying speeds and transmitted to the outer cylinder. This cylinder can rotate at a speed ranging from 0.001 to 1000 rpm. Its speed of rotation can be changed non-stepwise and linearly as required. The torsional oscillation or rotation of the outer cylinder is transmitted to the inner cylinder through the sample, and induces a shear stress at the surface of the inner cylinder. The resultant stress is converted into a torsional motion sufficient to equilibrate the rigidity of the torsion wire, and the motion converted into an electric signal by use of a differential transformer. In the dynamic method, a Lissajous' figure is drawn by the electric signals from the outer and inner cylinders using an X-Y recorder. An appropriate torsion wire meeting the viscosity of the sample is selected from among various diameters of wire. The size of the portion actually used for measurement is shown in Fig. 2. In this portion, the inner and outer cylinders are 4 and 5 mm in radius, respectively, with an effective depth of the sample 30 mm. Measurement can be made with about 1.5 ml of sputum.

**Method of measurement of dynamic viscoelasticity**

As shown in Fig. 1 (‡@ in the lower left-hand corner), a sinusoidal torsional oscillation with an amplitude of about 2 degrees is applied to the outer cylinder. The torsion angle of this cylinder is recorded on the X axis. The inner cylinder suspended with wire gives rise to an oscillation of the same period, exhibiting a phase difference. The resulting displacement, or torque, of this cylinder is plotted on the Y axis and recorded by the X-Y
Fig. 1. Diagram of the coaxial cylinder rheometer consisting of four portions (A) cylinder system, (B) driving mechanism, (C) a heat regulator, (D) a torque recorder.

Fig. 2. Dimensions of cylinders used in the coaxial rheometer. About 1.5 ml of sputum is enough to fill the space between the inner and outer cylinders completely.

Method of measurement of shear viscosity

The outer cylinder was subjected to a continuous speed-varying process in the same direction in a manner as to be almost expressible with an exponential function. It was rotated with an accelerated speed (presenting an ascending curve) at 0.1–300 rpm for about 13 min, and by a gradually reduced speed (presenting a descending curve) at 300–0.1 rpm for about another 13 min. Then the speed of rotation corresponding to the shear rate was plotted successively on the X axis, and the torque corresponding to this rate, or the shear stress, on the Y axis. In this manner the viscosity corresponding to each shear rate was calculated by the formulae given in the appendix.

Experiment 1 (the effect of stirring). Thirteen samples were collected from 11 patients with chronic bronchitis. They consisted of six, three, and four samples of purulent, mucopurulent, and mucoid sputum, respectively. The relationship between the macroscopic
appearances and the rheological properties of sputum in these samples was then studied. The samples of sputum were classified macroscopically by the grades described by Miller and Johnes (1963), in which M₁ was regarded as mucoid, M₂, P₁, and P₂ as mucopurulent, and P₃ as purulent.

First, by use of the thixotrometer, the dynamic viscoelasticity of the sputa was measured at seven points of an angular frequency. Next, using the same equipment, the steady flow properties were measured. Here the shear rate was accelerated continuously to a point and then reduced immediately to measure the shear viscosity continuously. Finally, the dynamic method was used again to determine the dynamic viscoelasticity. In nine samples (five purulent, two mucopurulent, and two mucoid) the dynamic viscoelasticity could be measured again after the determination of shear viscosity.

Each sample of sputum was kept at about 20°C until loaded into rheometer after having been collected at expectoration and measured within 4 hr after expectoration. Tests were made at 37.0±0.2°C.

Experiment 2 (pharmacological action). Purulent sputum obtained from patients with chronic bronchitis was mixed with a drug solution or distilled water (serving as control) at a ratio of 4:1, and stirred manually with a glass rod for 10 sec. In this manner we observed the changes in the rheological properties of sputum brought about by pharmacological action. The drugs tested were 20% N-acetyl-L-cysteine (NAC), 0.2% Bromhexine, and 0.5% semialkaline proteinase (Seaprose-S), which are a practical treatment for patients suffering an excessive production of sputum.

(a) Trial with 0.5% Seaprose-S. Measurement was carried out on 5 samples of sputum alone, 5 to which 0.5% Seaprose-S (the Seaprose group) was added 30 min before and 5 to which distilled water (the control group) was added 30 min before.

(b) Trial with 0.5% Bromhexine. Measurement was performed on 5 samples of sputum alone, 5 to which 0.2% Bromhexine (the Bromhexine group) was added an hour before and 5 to which distilled water (the control group) was added an hour before.

(c) Trial with 20% NAC. Measurement was carried out on 5 samples of sputum alone, 5 to which 20% NAC (the NAC group) was added 30 min before and 5 to which distilled water (the control group) was added 30 min before.
The measurement was done in a regular order, i.e., sputum to which an expectorant was added was measured first, followed by one to which distilled water was added, and finally sputum alone. In this study tests were made at a constant temperature (25.0±0.05°C) to avoid the effect of 'drying'. All the samples of sputum were examined within 4 hr after expectoration.

**RESULTS**

**Experiment 1**

Fig. 4 is a graphic representation of the relationships between dynamic viscoelasticity and angular frequency. These values were clearly dependent upon frequency; the higher the frequency, the smaller the value of the dynamic viscosity ($\eta'$) and the larger those of storage modulus ($G''$) and loss modulus ($G'$).

To determine whether there is a difference in the value of $\eta'$ or $G'$ according to the macroscopic appearance of sputum, the results of measurement in all the samples are presented collectively in Figs. 5 and 6. Samples of untreated sputum showed the trend that the mucopurulent and purulent samples exhibit a generally more elevated $\eta'$ and $G'$ than do the mucoid samples. However, this was a very small number of samples on which to base any conclusion regarding the correlation of $\eta'$ or $G'$ with sputum type.

After the measurement of dynamic viscoelasticity, shear viscosity was determined in all the cases studied. Fig. 7 shows hysteresis loops as a function of shear rate and shear viscosity. The area of hysteresis loop tended to be large in purulent sputum and small in mucoid and mucopurulent sputum.

Next, dynamic viscoelasticity was measured again in the samples of sputum in which shear viscosity had been determined. It was found that both $\eta'$ and $G'$ had increased two- to three-fold in two samples of mucoid sputum (Fig. 8). Of five samples of purulent sputum, four exhibited a reduction in $\eta'$ and $G'$ to about one

![Figure 4](image-url)
Fig. 5. Graph of dynamic viscosity presented by sputum of varying macroscopic appearance.

\( \circ \), mucoid; \( \bullet \), purulent; \( \circ \), mucopurulent.

Fig. 6. Graph of storage modulus presented by sputum of varying macroscopic appearance.

\( \circ \), mucoid; \( \bullet \), purulent; \( \circ \), mucopurulent.

Fig. 7. Comparison of the hysteresis loops in relation to shear rate and shear viscosity of three macroscopic types of sputum. It appears likely that hysteresis loops of purulent sputum (P) are larger than those of mucoid (M) and mucopurulent (M-P) sputum.
half their original values (Fig. 9), and the other one exhibited almost no changes in either $\eta'$ or $G'$. In one sample of mucopurulent sputum, $\eta'$ increased two- or three-fold and $G'$ remained almost constant (Fig. 10). In another sample of mucopurulent sputum, both $\eta'$ and $G'$ decreased to about one half their original values, and the sputum presented a behavior similar to that of purulent sputum.

Fig. 8. Graph of dynamic viscosity ($\eta'$) vs. storage modulus ($G'$) of a sample of mucoid sputum before (○—○) and after stirring (●—●). Both $\eta'$ and $G'$ increased after stirring.

Fig. 9. Graph of dynamic viscosity ($\eta'$) vs. storage modulus ($G'$) of a sample of purulent sputum before (○—○) and after stirring (●—●). $\eta'$ and $G'$ decreased after stirring.

Fig. 10. Graph of dynamic viscosity ($\eta'$) vs. storage modulus ($G'$) of a sample of mucopurulent sputum before (○—○) and after stirring (●—●). After stirring $\eta'$ increased and $G'$ remained almost constant.
Experiment 2

Trial with 0.5% Seaprose-S. Fig. 11 shows one of the five results of measurement of $\eta'$ and $G'$ conducted 30 min after addition of Seaprose-S or distilled water to sputum. All samples revealed results similar to those shown in Fig. 11, i.e., reduction in both $\eta'$ and $G'$ was much greater in the Seaprose group than in the control group.

Trial with 0.5% Bromhexine. Fig. 12 shows one of the five results of a comparison of $\eta'$ and $G'$ between the Bromhexine and control groups. All samples revealed results similar to those shown in Fig. 12. Here $\eta'$ is almost equal in both groups. The value of $G'$ tended to be slightly larger in the Bromhexine group than in the control group.

Trial with 20% NAC. When NAC was added to the sputum, agglomerations were formed, thereby making the resulting sample heterogeneous. Finally, an attempt was made in the NAC group to stir a sample manually with a glass rod for 20 sec before measurement of dynamic viscoelasticity. In the NAC group, $\eta'$ was larger than in the control group, and increased to almost the same value as that in the group of samples of sputum alone, especially with an increase in frequency. In the NAC group, $G'$ was smaller than in the control group. The difference in the value of $G'$ between the two groups was enhanced gradually with an increase in frequency. Fig. 13 shows one of the five results obtained by the dynamic method.

Fig. 11. Changes in dynamic viscosity ($\eta'$) and storage modulus ($G'$) of a sample of purulent sputum 30 min after addition of 0.5% Seaprose-S. The decrease in value of $\eta'$ and $G'$ is much greater than that of the control (distilled water).

- o, fresh sputum before addition of 0.5% Seaprose-S; o----o, sputum to which 0.5% Seaprose-S was added.
- - - - , fresh sputum before addition of distilled water;
- - - - , sputum to which distilled water was added as control.
Fig. 12. Changes in dynamic viscosity ($\eta'$) and storage modulus ($G'$) of a sample of purulent sputum 30 min after addition of 0.2% Bromhexine. Essentially the same degree of decrease in value of $\eta'$ and $G'$ is shown in this sample as in the control (distilled water).

○—○, fresh sputum before addition of 0.2% Bromhexine; ○—○, sputum to which 0.2% Bromhexine was added; •—•, fresh sputum before addition of distilled water; •—•, sputum to which distilled water was added as control.

Fig. 13. Changes in dynamic viscosity ($\eta'$) and storage modulus ($G'$) of a sample of purulent sputum 30 min after addition of 20% NAC. The values of $\eta'$ and $G'$ are larger and smaller, respectively, in this sample than in the control (distilled water). This difference is especially remarkable in the high-frequency range.

○—○, fresh sputum before addition of 20% NAC; ○—○, sputum to which 20% NAC was added; •—•, fresh sputum before addition of distilled water; •—•, sputum to which distilled water was added as control.
DISCUSSION

There is still controversy as to whether sputum viscoelasticity is different due to difference in macroscopic appearance of sputum. In the present study, it was impossible to classify the properties of sputum exactly by determining the value of $\eta'$ and $G'$ according to the macroscopic appearance of sputum. Mitchell-Heggs et al. (1974) pointed out that the elasticity of sputum at low shear rates did not differ significantly with macroscopic appearance. Sturgess et al. (1971), and Charman and Reid (1972) also found no significant difference between viscosity of purulent, mucoid, and mucopurulent sputum.

Purulent sputum usually contains a dense fiber network of DNA. At the same time, the fibers of acid glycoproteins appear markedly fragmented in the optical microscope (Bürgi 1973). On the other hand, mucoid sputum contains only a few DNA fibers and, above all, less bacterial enzymes or protein which could combine with glycoprotein fibers (Bürgi 1973). Mucoid sputum is therefore governed by glycoprotein fibers and purulent sputum by DNA fibers. The reason for the lack of differences in viscoelasticity between purulent and mucoid sputum in spite of their different fiber-like structures, as mentioned above, is not clear, but our results suggest it is unlikely that the physicochemical properties explain the significant correlation with dynamic viscoelasticity. Puchelle et al. (1973), Rosenbluth and Chernick (1974), and Picot et al. (1978) also noticed that there was no relation between viscosity and DNA content.

By contrast, Bruce and Quinton (1962), Feather and Russell (1970), and Palmer et al. (1970) reported from their studies on chronic bronchitis that mucoid sputum was more viscid than purulent. Such discrepancies in results may be explained partly by the process performed before measuring viscosity. Up to the present the viscosity of sputum has frequently been measured on a sample homogenized by stirring. Several investigators (Bonomo et al. 1968; Turgeon et al. 1969) reported that homogenization of sputum by ultrasonic disintegration or treatment with a Potter pestle decreased shear viscosity, but they did not investigate
changes of dynamic viscoelasticity in the differences in the macroscopic appearance of sputum. On the other hand, Sturgess et al. (1971) reported that shearing sputum at a low shear rate (up to 10 sec\(^{-1}\)) and then allowing it to stand between the platens for one hour produced a striking increase in dynamic viscosity, which did not occur if sputum was left on the bench without previous shearing or if shearing was carried out at higher rates. However, the effect of stirring on sputum elasticity was not investigated. After a sample of sputum was used for measurement of shear viscosity in the present study, it was assumed to have been homogenized by stirring. Nevertheless, the dynamic viscosity and storage modulus of the stirred sputum were completely different in behavior from those of the same sputum before stirring in accordance with the macroscopic appearance of sputum: when they were stirred sufficiently, dynamic viscosity and storage modulus increased in mucoid sputum and decreased in purulent sputum. Therefore, the result of Bruce and Quinton (1962) who studied the sputum already sheared before measuring viscosity is open to question. The conventional method of measurement of stirring is something which may need to be reexamined. These results may be caused by variation in the rigidity of the fiber-like structure as well as by their crosslinking to form a lattice varied by stirring, which may vary in intensity with the macroscopic appearance of the sputum.

The dynamic behavior of sputum is one of the indicators of readiness of expectoration. From a rheological point of view, it must be understood as a combination of at least two factors, viscosity and elasticity. It follows, therefore, that an expectorant must modify the rheological properties of mucus in the bronchial lumen such that the mucus will be in an optimal condition for transport by ciliary movement. It has been reported that the number of beats of a single cilium is 1,000±200 c/min for the frog, 876±151 c/min for the cat, and 1,317 c/min for the rat (Dulfano and Adler 1975). Therefore, the number of beats is about 20 c/sec, regardless of the species of the animal. The thixothrometer used in the present investigation could be used only for a relatively narrow range of measurement of angular frequency from 0.01 to 1.0 rad/sec (from 0.0016 to 0.16 c/sec), and it was not capable of measuring a frequency of about 20 c/sec. The present investigation, although it was performed at a lower shear rate than that of a single cilium, revealed the presence of three types of expectorants: (1) a drug which reduces both dynamic viscosity and storage modulus to a large extent (Seaprose-S), (2) a drug which exerts little influence upon dynamic viscosity and increases storage modulus slightly (Bromhexine), and (3) a drug which increases dynamic viscosity a little and reduces storage modulus to a large extent (NAC).

Seaprose-S, a proteinase which is used orally, may be transferred into the bronchial lumen from the blood stream to act directly upon sputum. Therefore, changes in the viscoelasticity of sputum by administration of this drug may be predicted from the results of in vitro experiments. It is said that proteolytic enzymes have less effect on purulent sputum than on mucoid sputum, possibly because DNA contributes to the viscosity of purulent sputum and also inhibits
proteolysis (Lieberman et al. 1965; Lieberman 1967). Nevertheless, in the present study, the viscoelasticity of purulent sputum to which Seaprose-S had been added decreased markedly. The greater effectiveness of this drug on mucoid sputum viscoelasticity may be expected, and probably results from the fact that the proteolytic enzyme decomposes high-molecular weight proteins in sputa, causing significant changes in the composition of the sputum.

As for Bromhexine, Mastella et al. (1970) carried out studies in vitro by use of Brookfield’s cone-plate viscometer, but could not demonstrate a reduction in viscosity, regardless of the macroscopic appearance of the sputum. In the present investigation no dynamic viscoelasticity was reduced in any sample of sputum to which Bromhexine had been added. Therefore, it is suggested that the mechanism of dissolution of sputum by administration of this drug probably does not entail any direct action of the drug itself. In fact, electron microscopic findings (Gieseking and Baldamus 1968) suggest that the lytic effect of Bromhexine is mainly due to enzymatic processes induced by lysosome-like granules, which under the influence of this remedy are in considerably increased quantities supplied by the serous epithelial cells of the bronchial glands.

It has been demonstrated that the mechanism of the action of NAC is due to the breaking of the disulfide bonds of the mucoprotein. Sheffner (1963) reported that the viscosity of human pulmonary secretions containing deoxyribonucleic acids was markedly reduced by treatment in vitro with N-acetyl-L-cysteine. On the other hand, Mastella et al. (1970) reported that the viscosity increased in purulent and mucoid sputum, and decreased in mucopurulent sputum after 10% NAC aerosol inhalation. They did not discuss, however, the dynamic viscosity or storage modulus of sputum. In the present investigation, agglomerations were produced in sputum to which NAC had been added. In some samples they were broken by stirring to prepare homogenized specimens; in others they were not. It was then noticed that there was a large difference in measurements between the homogenized samples and those containing agglomerations. Our work deals only with the results of samples homogenized by slight to moderate stirring. The degree of stirring is important because experiment 1 demonstrated that dynamic viscosity and storage modulus decreased markedly in purulent sputum when they were stirred sufficiently. The appearance of such a difference indicates that ample care must be taken in handling samples of sputum. Even when a sample of sputum to which NAC had been added was homogenized by means of an intense external force, the decrease in viscosity was less distinct than that in elasticity (unpublished data). This is probably because elasticity was reduced when the fragile structure of sputum was destroyed and the resulting finely broken fragments of sputum were dispersed in the liquid layer to exhibit a viscosity enhanced to some extent.

Thus the mechanism of action of these expectorants is not expected to be the same either in vivo or in vitro. Accordingly, it is very difficult to discuss the effect of each drug as an expectorant simply on the basis of the results obtained from the in vitro experiments. Regardless of the mechanism of action, however, an
expectorant eventually changes the viscoelastic behavior of mucus in the bronchial lumen, thereby facilitating removal. In the present investigation the rheological properties of sputum to which an expectorant had been added showed patterns of change depending upon the type of expectorant used, which is notable interest. Further studies will be necessary in order to determine in vivo the effect of these drugs on the viscoelasticity of sputum and to estimate their clinical significance.

APPENDIX

(I) Method of determination of the phase angle from the Lissajous’ figure (Fig. 14)

Phase angle \( \phi \)

\[ \sin \phi = \frac{\text{Area of ellipse}}{\text{Area of circumscribed quadrangle}} \times \frac{4}{\pi} \times \frac{ab}{\theta \times \theta} \]

Amplitude ratio: \( m = \frac{\theta}{\theta} \)

(II) Formulae for calculation of dynamic viscosity and complex modulus

a) real part of complex modulus

\[ G' = -\frac{m(m - \cos \phi)}{1 - 2m \cos \phi + m^2} \cdot \frac{1}{R_1^2 - R_2^2} \cdot \frac{1}{4\pi h} K \text{ (dyne/cm)}^2 \]

b) imaginary part of complex modulus

\[ G'' = \frac{m \sin \phi}{1 - 2m \cos \phi + m^2} \cdot \frac{1}{R_1^2 - R_2^2} \cdot \frac{1}{4\pi h} K \text{ (dyne/cm)}^2 \]

c) dynamic viscosity

\[ \eta' = \frac{m \sin \phi}{1 - 2m \cos \phi + m^2} \cdot \frac{1}{R_1^2 - R_2^2} \cdot \frac{1}{4\pi h} K \cdot \frac{1}{\omega} \text{ (poise)} \]

\( R_1 \) and \( R_2 \): Radius of the inner and outer cylinders, respectively (cm)
\( h \): Height of the inner cylinder (cm)
\( \omega \): Angular frequency (rad/sec)
\( k \): Torsion constant of wire (dyne·cm/rad)

(III) Formulae for calculation of shear viscosity

\[ \eta' = \frac{T}{4\pi h \omega} - \left( \frac{1}{R_1^2} - \frac{1}{R_2^2} \right) = \frac{k\theta}{4\pi h \omega} \cdot \frac{1}{R_1^2} - \frac{1}{R_1^2} \text{ (poise)} \]
Shear rate $= \frac{2\omega}{1 - \frac{R_1^2}{R_2^2}}$ (sec$^{-1}$)

$T$: Torque at the surface of the inner cylinder (dyne·cm)
$\omega$: Angular velocity of the outer cylinder (rad/sec)
$k$: Torsion constant of wire (dyne·cm/rad)
$O$: Angle of rotation of the outer cylinder (rad)
$h$: Height of the inner cylinder (cm)
$R_1$ and $R_2$: Radius of the inner and outer cylinder, respectively (cm)

References


