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New equipment for measurement of the force of adhesion of mucoadhesive films

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New equipment for measurement of the force of adhesion of mucoadhesive films

We declare that the study was performed according to the international, national and institutional rules.
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We have had the English of the text checked by a scientist whose mother tongue is English.

The authors have no conflict of interest to declare.

Yours sincerely,
Klara Pintye-Hódi

New equipment for measurement of the force of adhesion of mucoadhesive films

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Abstract

A better recognition of the properties of materials is of great interest in pharmaceutical technology, and especially in the development of modern solid dosage forms. As an example, a knowledge of the force of adhesion of a mucoadhesive preparation is of considerable importance. The aim of the present study was to develop calibrated equipment suitable for determination of the force of adhesion and for following the process of film deformation during testing. A new instrument is introduced, and results are presented.

Keywords: adhesion, polymer, hydroxy propyl cellulose, Klucel ®MF, mucoadhesive films

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1. Introduction

As a consequence of their advantages [1], mucoadhesive therapeutic preparations (tablets, films, patches and gels) are at currently the focus of research work. The buccal region of the mouth is a possible area for drug penetration, when the "first-pass effect", the acidic pH of the stomach and the action of different enzymes in the gastrointestinal tract may be avoided. This is a popular mode of administration for the patients, and especially children, because the preparations are small and flexible, and easy to apply. The level of patient compliance may therefore be appropriate. During application, the mucoadhesive film should be carefully placed in the mouth and pressed gently with one finger onto the mucosa for several seconds until weak chemical bonds are formed between the polymer and the mucin chains, and the film adheres to the mucosa. Three processes are involved: 1. the wetting and swelling of the polymer, 2. the penetration of moisture into the polymer, and (3) the formation of weak chemical bonds between the chains [2]

The applicability of this form of therapeutic administration demands a knowledge of the force of adhesion of the mucoadhesive dosage form.

The authors deal more times with the adhesion of transdermal drug delivery system [3], but the literature reveals that the measurement of the force of adhesion of mucoadhesives is not uniform. Various methods have been utilized [4, 5-13], and instruments used have included a viscosimeter [4], an ellipsometer [6], a shear test [10], a texture analyser [11], a dynamometer [12], a modified balance [13], etc.

Our work has focused on the preparation and investigation of mucoadhesive films, and we have developed calibrated equipment suitable for determination of the force of adhesion, which also allows the process of film deformation to be followed during testing. The novelty of this system is that the total deformation curve of the sample can be analysed.

2. Experimental

2.1. Equipment

The equipment used to measure the forces of adhesion of polymer films was based on the hardness tester described in detail earlier [14].

The pressure is measured through the use of a load cell connected to a locally developed digital acquisition (DAQ) box. This is based on the Silicon Laboratories C8051F124 microcontroller kit. During the measurement, the DAQ box sends the acquired data to the PC side software via an RS232 connection. With this device, the start of data acquisition is controlled manually because the pressure jowl must be positioned exactly on the surface of the material. The end of the data acquisition is also controlled manually, because the breaking point of relatively elastic materials such as films can not be detected exactly.

The original embedded software of the DAQ box was modified in order for it to be suitable for the measurement of forces of adhesion. The adhesion force measurement algorithm performs the following operations:

- At the beginning of the measurement process the pressure jowl moves downwards and presses against the polymer film until it reaches the predefined pressure force (static pressure force).
- It holds its position until the desired timeout (static pressure time).
- At this time, the pressure jowl begins to move upwards until the user stops the measurement process (dynamic pressure force).

The two parameters which can be set up freely in the algorithm (the static pressure force and the static pressure time) have to be set before the measurement via the PC side software (Figure 2).

The measurement range was 0–200 N, the speed of the stamp was 20 mm/min, and the output was 0–5 V. The sensor was a Unicell force-measuring instrument, calibrated with the C9B 200 N cell.

2.2. Materials

Hydroxy propyl cellulose (Klucel MF) (Aqualon; Hercules Inc., Wilmington, USA) was used as film-forming material and glycerine (Ph Eur) as plasticizer.

2.3. Preparation of free film

2 w/w% film-forming polymer was used in aqueous solution. The films were made by casting technology on a Teflon surface. The samples were dried in the air at room temperature (25 ºC/60 RH%) for 24 h.

2.4. Storage of films

The films were stored in a climate chamber at 40 °C/50 RH% during a week.

2.5. Measurement of force of adhesion

The structure of the measurment system was as follows, from top to bottom: a stainless steel holder, a bilayer adhesive tape, a film, mucin gel and a stainless steel table. Each element was measured alone, in pairs and all together. Before the adhesion test, each film was subjected to 50 N, held for 45 s, and the holder then pulled up the film up from the mucin gel layer.

A minimum of 10 parallel measurements were made.

3. Results and Discussion

The total deformation process involved in the measurement of the force of adhesion of a film is illustrated in Figure 3 It displays not only the adhesion force value, but the process The recoil of the spring under the stainless table can be seen at the beginning of the curves. During the pressing procedure, every non-steel part of the system (the bilayer adhesive tape, the mucin and the film) undergoes a deformation;, section 1 of the curves reflects these phenomena. The almost horizontal parts of the curves (section 2) relate to the period when contact with the bottom at 50 N is maintained for 45 s. After the 45 s holding time, the motor is reversed and starts to pull up the film. This is shown by the vertical line, followed by a 2-s pause. The peaks in the last part of the curves (section 3) relate to the force of adhesion which covers the elastic recovery of the sample (the bilayer adhesive tape, the mucin and the film together). Finally, correction for the forces of adhesion of the tape and mucin alone leads to the force of adhesion of the sample: 18.1 N.

The software also permits magnification of the different sections of the curve, and it is therefore possible to study the deformation of the samples better, especially in sections 1 and 3 (Figures 4 and 5).

Figure 4, depicts the initial deformation of a sample during static loading, with a short elastic and longer plastoelastic deformation.

Figure 5 demonstrates the deformation during the dynamic (tensile) process when the force of adhesion is involved. The curve indicates elastic behaviour until the termination of the adhesion. The descending section shows that the contact between the mucin and the film is partially broken.

4. Conclusions

This work has revealed that this equipment with the new software, which is suitable for study of the deformation of a mucoadhesive film successively during static loading and constant loading, and for determination of the force of adhesion. There results demonstrate that the characterization of mucoadhesive films is possible. The results were utilized to create a theoretical model suitable for prediction of the optimum film composition that ensures the required adhesion to the mucous membrane.

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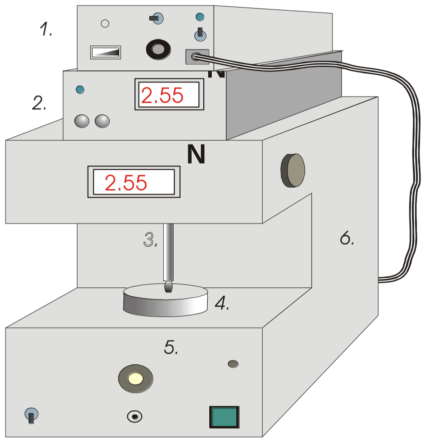
The authors have no conflict of interest to declare

Figure



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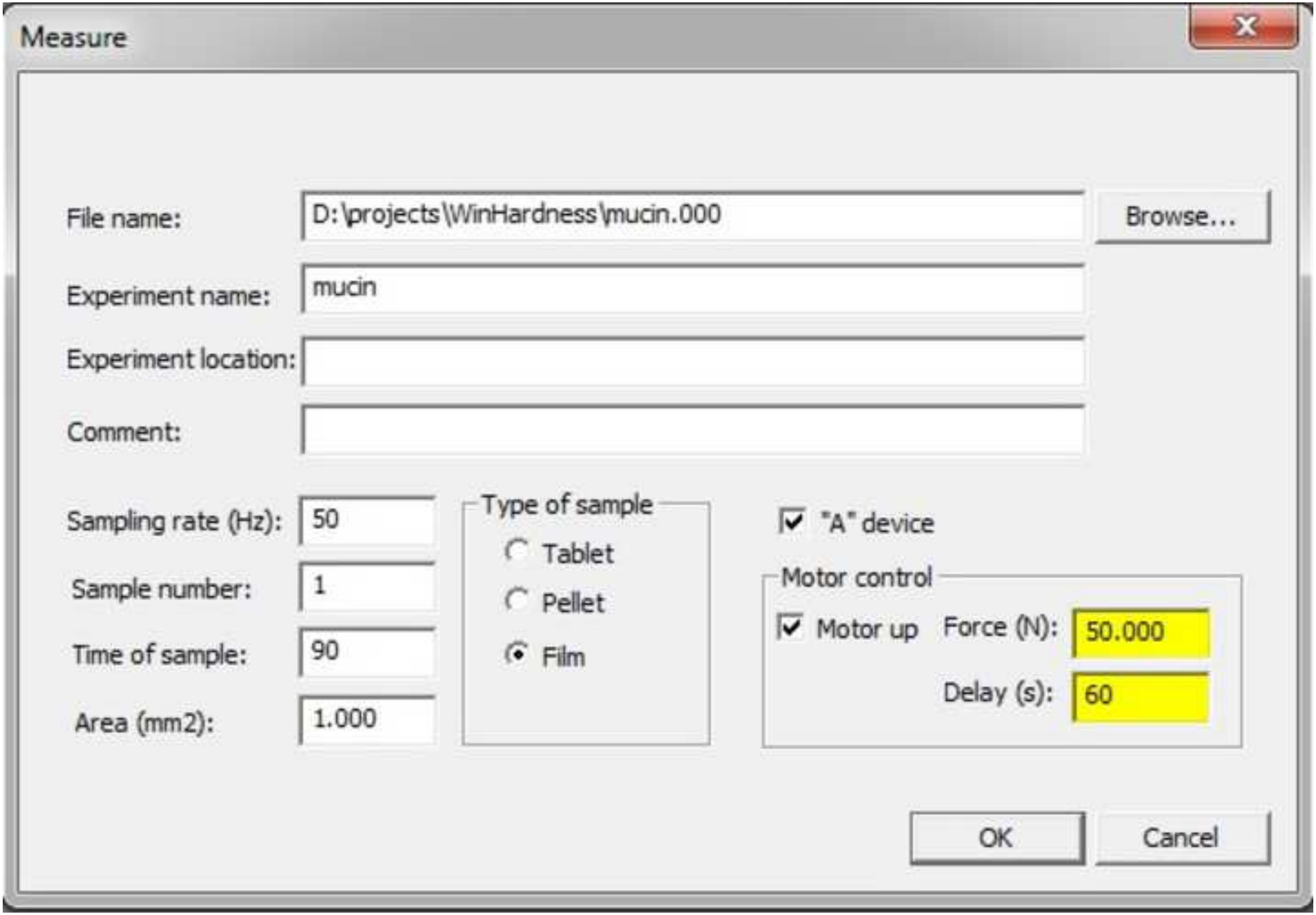

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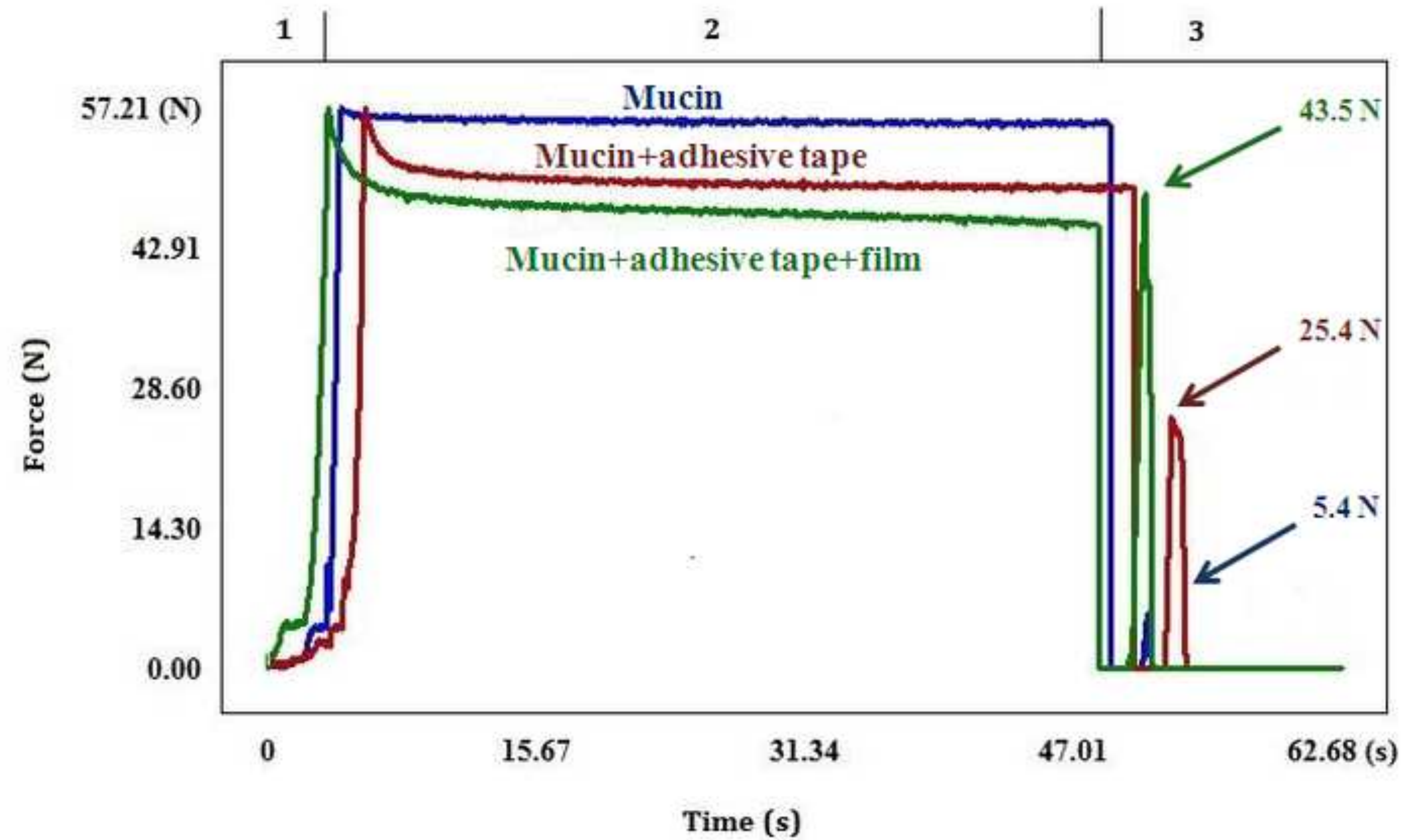

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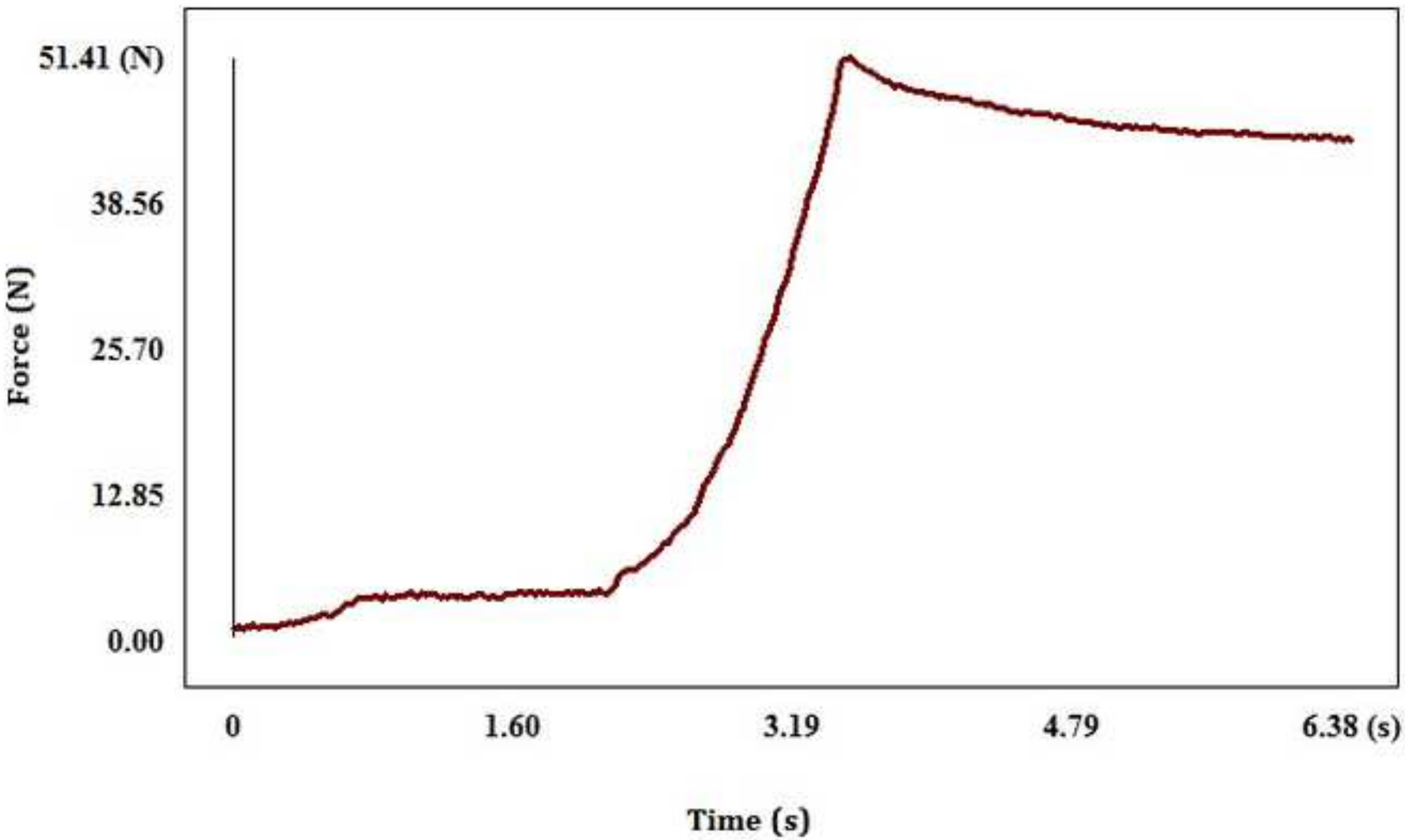

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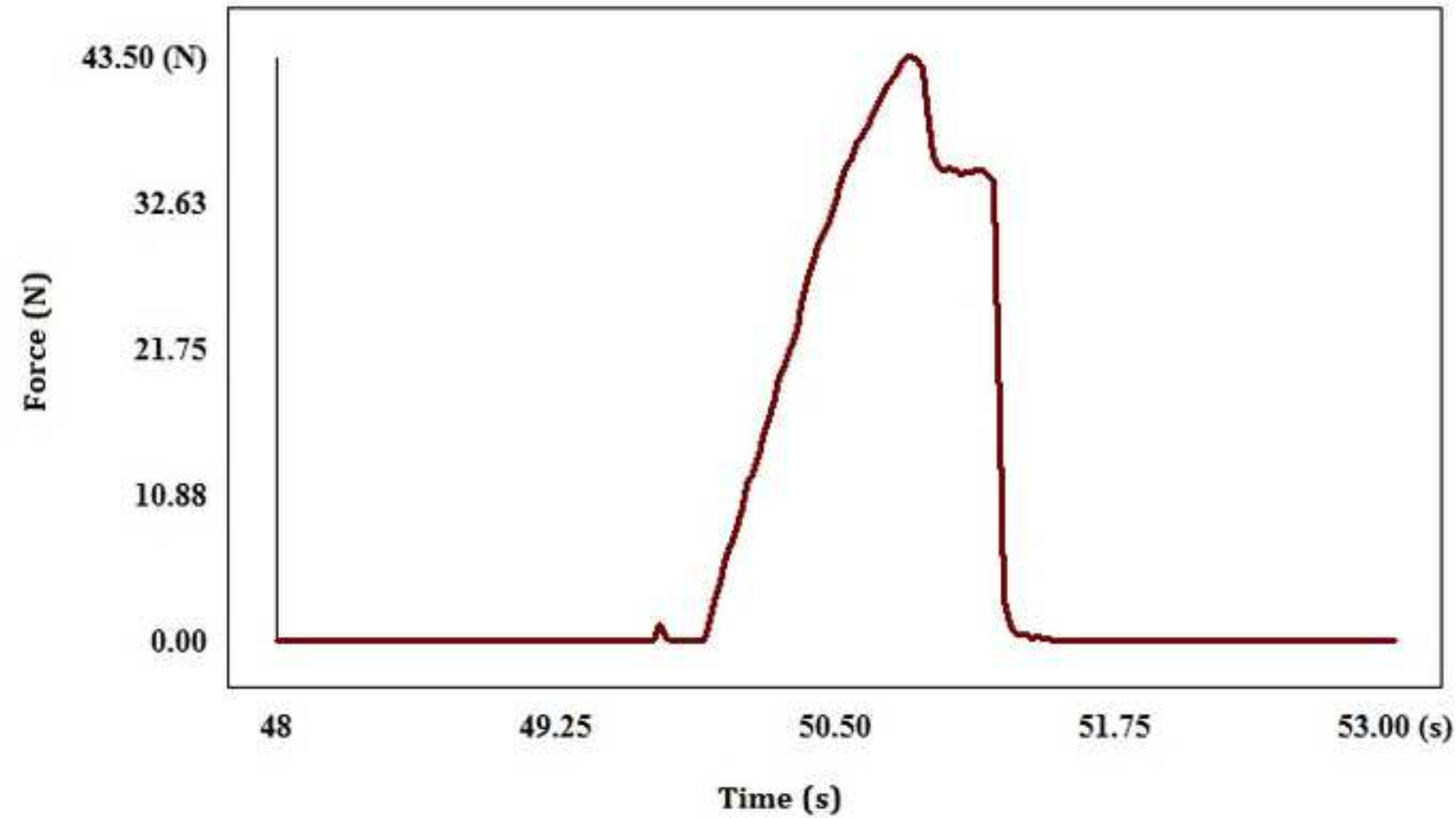

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