Thermo Haake
Material Characterization

The Rheological Characterization of Thixotropic Pharmaceutical Products

Introduction

Thixotropic pharmaceutical products that are applied from a tube are usually in the form of a salve or gel. Successful application of the substance requires that only minimal force is necessary in squeezing the product from the tube, and that the substance ultimately remains where it is applied.

In a rheological sense, it is important to characterize the thixotropic properties (i.e., the time dependent behavior) and also the yield stress. The substance should retain the original yield point so that it doesn't drip from the applied surface, and after application, the substance should regenerate its original consistence as quickly as possible. It is also important that the thixotropic structure is readily destroyed upon spreading the substance.

It is possible to measure the following properties with the HAAKE RV20/CV20:

I. The thixotropic breakdown with a flow curve or time curve.

II. The regeneration characteristics after the thixotropy has been destroyed.

III. The yield stress.

Instrument Description

The instrument combination used consisted of the base unit Rotovisco RV20, the Rheocontroller RC20 which acts as an interface between the computer and Rotovisco RV20 and the measuring system CV20 utilizing a cone-and-plate geometry. A HAAKE circulator provided precise temperature control for the samples.

HAAKE CV measuring systems are based on the Couette principle. This simply means that the plate (or cup) is driven by an electronically regulated motor and the resulting torque is measured at the stationary cone (or rotor). It is possible to measure a precise and inertia-free torque by separating the drive and torque sensor in the above manner.

Torque measurement is accomplished with a sensor system directly fastened to an extremely stiff torsion element with a maximum deformation of 0.3°. Since the sensor system and torsion bar are directly fitted together, usual measuring errors due to bearing friction are non-existent. It is further possible with such a measuring system to make practically non-destructive viscoelastic measurements at a very small oscillating strain.

The rheometer can be automatically controlled by software available from HAAKE. Software possibilities include Rotation, Oscillation and Normal Stress.

Fluids as well as pastes can be measured in the Couette system with a proper choice of sensor geometry. Possibilities include double gap cylindrical, concentric cylinders, Mooney-Ewart, cone-and-plate and parallel-plate. Test samples can be measured between 5 and 95°C with the aid of a precise circulator such as the HAAKE F3-C.

In the present study, a cone-and-plate geometry is employed. The stationary cone is truncated as shown in Figure 1. The cone is positioned such that the theoretical cone tip touches the plate in order to properly calculate the shear rate in the gap. This configuration makes it possible to measure substances that contain particles up to a size of 60 μm.

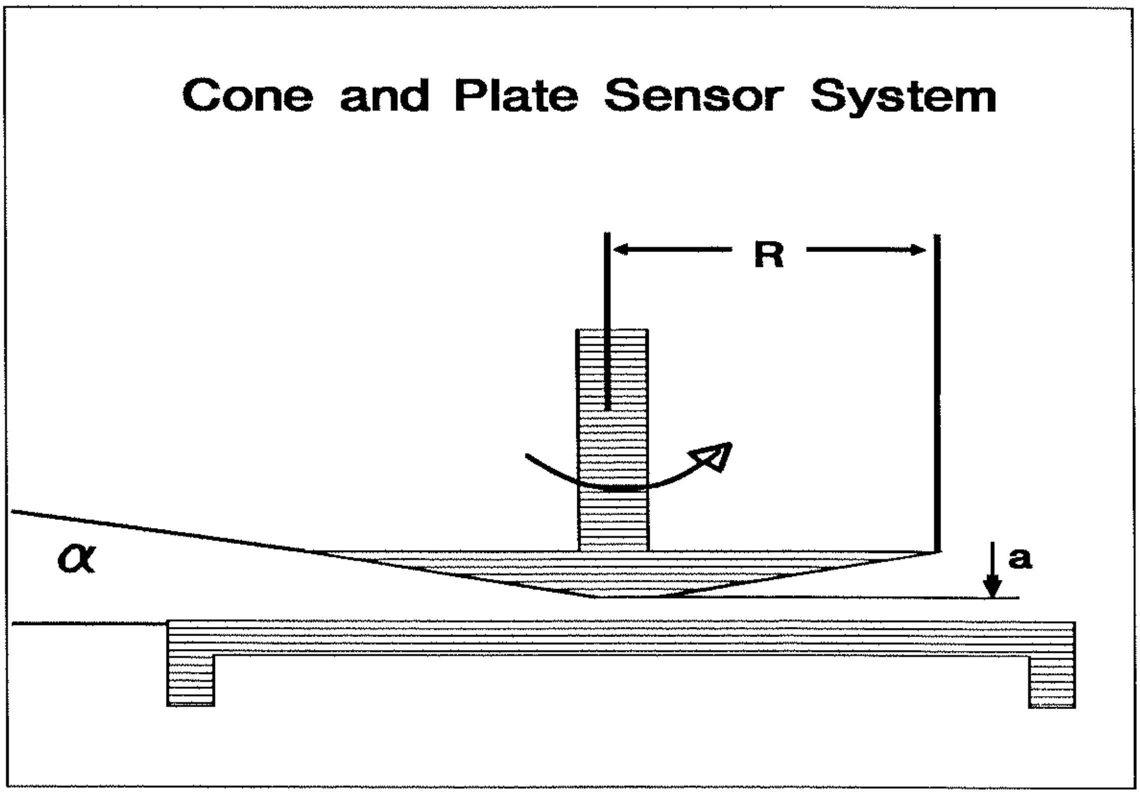

Figure 1. Diagram of a truncated cone-and-plate sensor system.

After placing the test sample on the plate, the measuring head is lowered on to it. The shear rate (speed) is the assigned test parameter and the resulting torque measured electronically according to the displacement of the torsion bar. The absolute viscosity can be subsequently calculated from the parameters speed, torque and measuring geometry.

Experimental Outline

The characterization of thixotropic pharmaceutical products can be differentiated into three methods of measurement. The first method consists of measuring the flow curve from zero to a pre-determined maximum shear rate, and after a set holding time with the aim of minimizing the thixotropic structure, measuring a flow curve back to zero shear rate. If a hysteresis exists between the ascending and descending curves, the substances can be described as thixotropic and the area between the curves corresponds to the amount of thixotropy.

The second method consists of measuring the regeneration characteristics. The sample is first sheared continuously for a pre-determined time at a high shear rate in order to destroy the thixotropic structure. The shear rate is then dropped to a low value and the subsequent increase of the shear stress tracked as a function of time (i.e. structure regeneration). The lowest possible shear rate should be chosen so that straining of the regenerating structure is minimized.

The third method is to determine the yield stress, which is a measure of the force necessary to make the resting substance flow.

In order to measure the yield stress, it is necessary to run a flow curve at the lowest shear rates possible and to measure the resulting shear stress (i.e., from 0 to 0.1 1/s in 2 minutes).
Since the yield point is dependent on the intensity and time of the applied strain, especially in the case of thixotropic materials, the same experimental parameters should always be used in order to obtain good reproducibility.

Experimental Results

Two gels which visually appear to have the same properties were tested and the flow curves are shown in Figure 2.

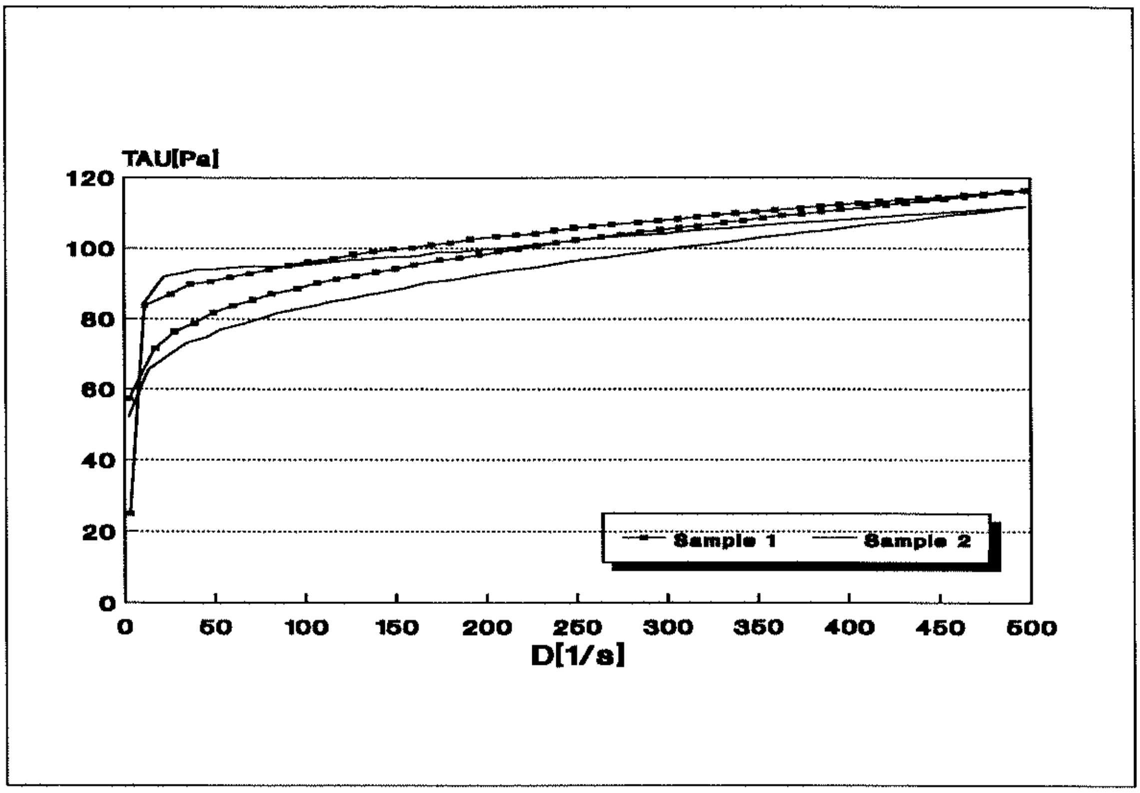

Figure 2. Comparison of the flow curves for two different gels.

Both samples reveal that the thixotropy is greatest in the low shear rate region. Sample 1 has a higher degree of thixotropy than sample 2 as evidenced in the hysteresis between the ascending and descending curves. This result ultimately signifies that sample 1 is easier to spread.

The regeneration behavior of the two test samples as a function of time is shown in Figure 3. Both gels regained 90% of their structure after 0.9 minutes.

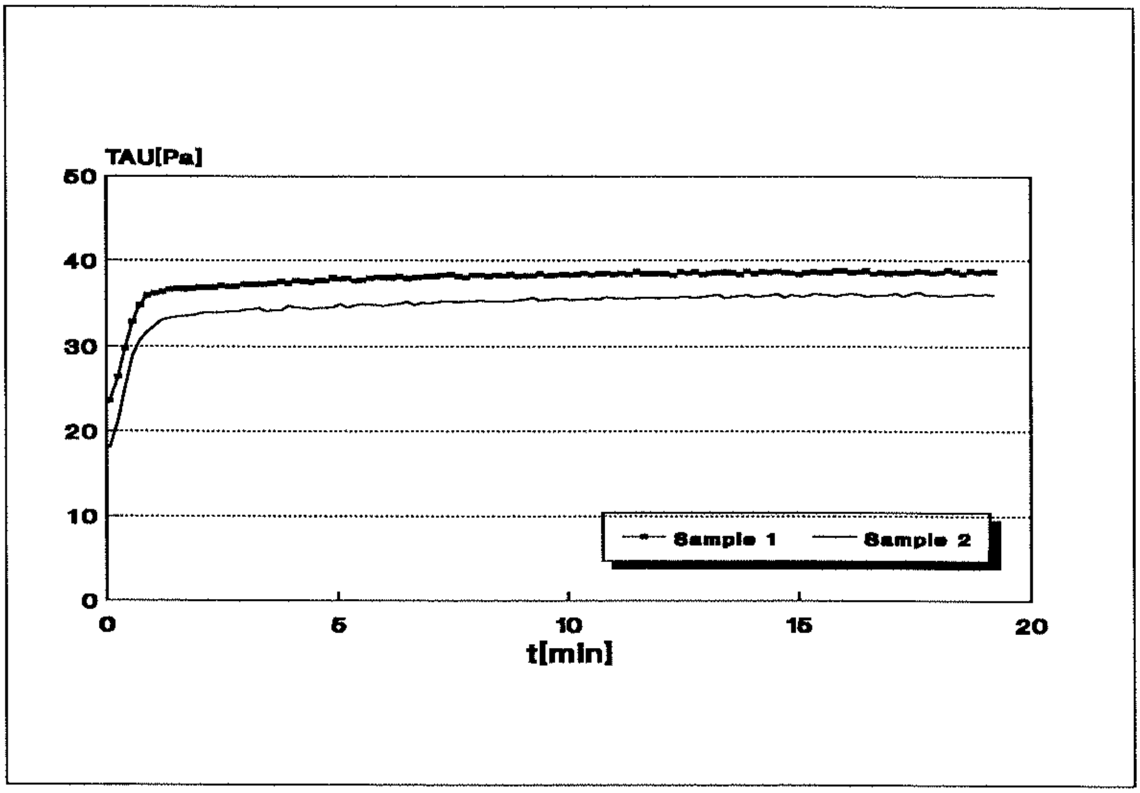

Figure 3. Comparison of the regeneration times of both gels.

This result implies that after exiting the tube, the gel will not drip and will behave as a quasi-solid body when at rest or low strain.

The shear stress behavior at a low shear rate is shown in Figure 4. The yield stress is equivalent to the shear stress at which the curve reaches a plateau. It is evident that more force is initially required to make sample 1 flow (i.e., to squeeze from the tube).

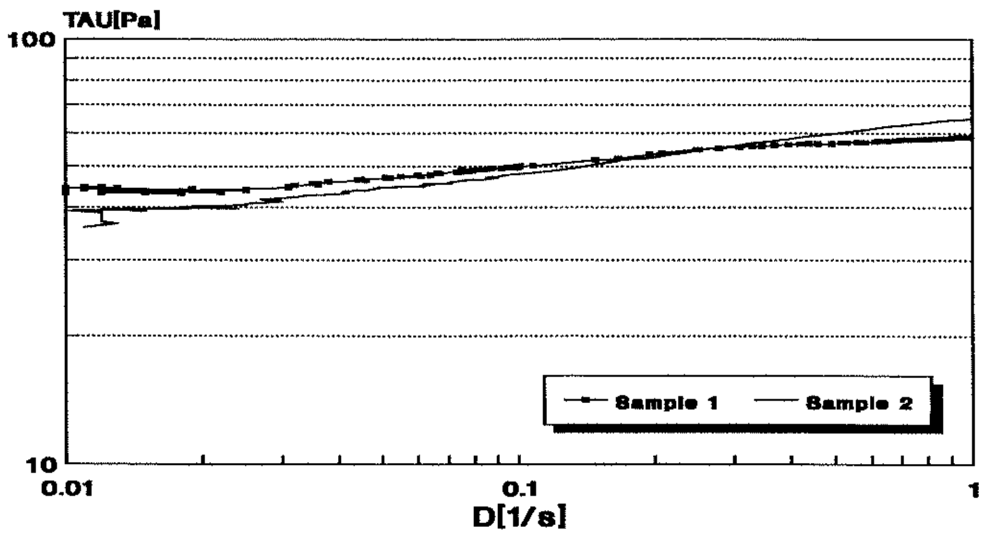

Figure 4. Comparison of low shear behavior.

International
Thermo Haake
Dieselstr. 4. 76227 Karlsruhe
Germany
Tel. +49(0)721 40 94-0
Fax +49(0)721 40 94 300
Hotline +49(0)18 05 04 22 53
info@thermohaake.com
www.thermohaake.com

USA
Thermo Haake
5225 Verona Road
Madison, WI 53711
Tel. 608-327-6777
Fax 608-273-6827
infousa@thermohaake.com
www.thermohaake.com

France
Thermo Rheo
99 route de Versailles
91160 Champlan
Tel. 01 64 54 01 01
Fax 01 64 54 01 87
info@thermorheo.com
www.thermorheo.com