QUALIFYING FLOW BEHAVIOR FOR PHARMACEUTICAL OINTMENTS

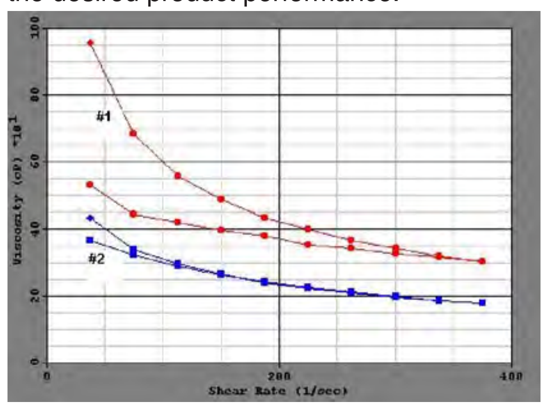
Pharmaceutical ointments are engineered to have rheological properties important to the physical performance of the product when used by the consumer. Most ointments are intended to be thick when standing to prevent them from flowing away from the intended area of use. High viscosity at near zero shear rate characterizes this behavior; determining the yield stress value quantifies this desired property. Ointments are also engineered to be easy to apply when rubbed. This is known as shear thinning behavior. Both characteristics of yield and shear thinning can be easily determined using only a small volume of sample with a Cone/Plate Rheometer.

The test method involves running a shear rate ramp. For example, a Brookfield DV-III Ultra Cone/Plate Rheometer (see **Figure 1**) with cone spindle CPE-40 enables low to high shear rate measurements with only 0.5mL of sample material (see **Figure 2**). Temperature control of the plate is easily accomplished by connecting the sample cup to a circulating water bath. With the sample in place on the plate inside the cup, a few minutes are allowed to achieve temperature equilibrium of sample with plate and spindle. Then the Rheometer is run from 0 to as high a shear rate as practical. The low shear rates typify slow movement of the ointment; perhaps a slow squeezing action coming out of the tube, while the higher shear rates reflect the rubbing action to apply the ointment to the skin.

Figure 1 / Wells/Brookfield DV-III Ultra Cone/Plate Rheometer

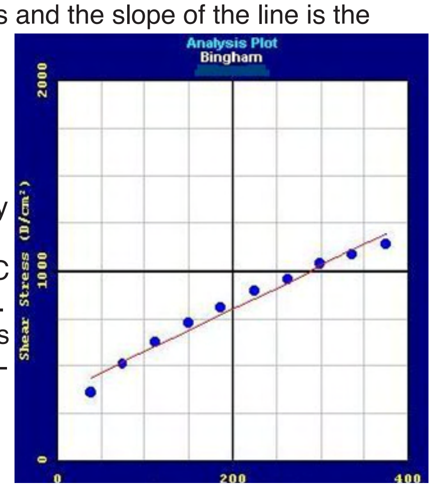
Figure 2 / *Sample Cup Spindle for Wells/Brookfield Cone/Plate Instrument. Sample Goes On Plate Inside Cup. Ports On Cup Connect To Circulating Temperature Bath.*

Rheocalc Software allows total control of the DV-III Rheometer from a PC. With the new "Secure Mode" feature in the latest version of rheocalc, the test method cannot be altered, once established by Engineering or Quality Control. When running the test, the viscosity data is automatically collected. Again, the "Secure Mode" feature prevents any modification of the test results. Graph 1 shows viscosity profiles of two ointments whose physical appearance is similar. However, a single, programmed viscosity test clearly demonstrates significant difference between the two. The graph shows viscosity measured during a shear rate ramp for 37 sec^{-1} up to 375 sec^{-1} then back to the starting value. The entire measurement time was 6.5 minutes. While both samples exhibit shear-thinning behavior, Sample #1 shows a significant loss of viscosity as a result of shearing action, while Sample #2 shows minor viscosity loss. Loss of viscosity due to shearing action is termed "thixotropy." Such tests allow the pharmaceutical manufacturer to adjust formulations to consistently achieve the desired product performance.



Graph 1: Viscosity vs. Shear Rate Data For Two Pharmaceutical Ointments

The Brookfield Rheocalc software enables data acquisition and storage as well as the ability to fit rheological math models to the data to estimate parameters such as yield (the shear stress required to initiate flow) and plastic viscosity (the function of shear stress required to maintain constant flow). In **Graph 2**, a Bingham analysis has been performed; this math model is one of several included with Rheocalc. The intersection of the "best fit" line with the y-axis is the yield stress and the slope of the line is the plastic viscosity. The new capabilities afforded with the "Secure Mode" Rheocalc software provide the pharmaceutical industry with a much-needed low-cost solution for QC viscosity measurement. Additional information is available at www.brookfieldengineering.com.



Graph 2: Bingham Math Model Used On One Of The Data Sets Shown In Graph 1

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