

SHELF LIFE: DOES VISCOSITY MATTER?

Medicinal mixtures administered by drinking or injecting the solution may in some cases contain special purpose additives that are in suspension, not in solution. The carrier liquid requires properties that suspend the additives and prevent settling over time due to influence of gravity. Pharmaceutical manufacturers perform shelf-life studies to verify product performance, ensuring that the additives do not settle out within the prescribed period for use of the mixture.

The carrier liquid is treated with thickening agents that provide these suspension properties for the additives. Testing the viscosity of the carrier liquid alone is one way to predict the behavior of the mixture before the inclusion of the additives. A flow curve test run at low shear rates (0.1 to 1.0 inverse seconds) can approximate the situation of product on shelf. (See **Figure 1**)

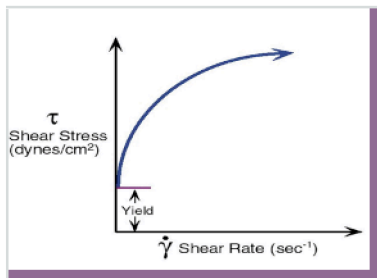


Figure 1: Plot of Shear Stress vs. Shear Rate to Determine Yield Stress in the Carrier Fluid

By plotting shear stress against shear rate, the yield stress of the carrier fluid can be determined. Back-calculating the stress to zero shear rate gives a value for the Yield Stress in the carrier fluid.

Flow curve testing at medium to high shear rates (10 to 1000 inverse seconds) simulates movements the carrier liquid might experience during transport from the manufacturing plant to store shelf. (See **Figure 2**) The viscosity will reduce as shear rate is increased, but should then recover as the shear

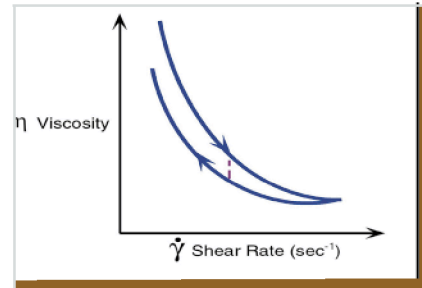


Figure 2: Plot of Viscosity vs. Shear Rate to Evaluate "Recovery" of Carrier Liquid Viscosity during Shaking and Vibration.

rate returns to zero. Rapid recovery of viscosity is important because it ensures that the suspension property of the carrier liquid will not diminish with shaking and vibration.



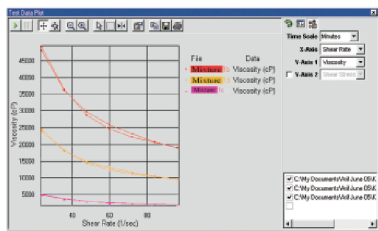
Figure 3: Brookfield Cone/Plate Rheometer for Evaluating Viscosity Behavior of Medicinal Mixtures

A Cone/Plate Rheometer is the type of instrument that can perform both of the above tests. (See **Figure 3**) Sample size required for testing is small, which can be an important consideration

when the medicinal mixture is expensive. Temperature control is easily accomplished by connecting the sample cup ports to a circulating temperature bath. (See **Figure 4**) Evaluating test sample behavior for variable temperature conditions is another important consideration, but will not be discussed further in this article.



Figure 4: Detailed View of Cone Spindle and Sample Cup with Ports for Connection to Circulating Water Bath



Use of software to run repeated Cone/Plate tests on retained samples is important as part of the shelf life evaluation process.

Figure 5:
Brookfield Rheocalc Software Provides
Viscosity Test Data for Shelf-Life Evaluation

(See Figure 5) The software provides the flexibility to run multiple types of tests automatically and as often as is required. The elimination of operator involvement guarantees that the tests are run identically each time. Data capture is complete and comprehensive. Security features guarantee integrity of data.

Pharmaceutical manufacturers are universally aware that “reasonable” product shelf-life is necessary to ensure market acceptance. What may be a new revelation is that product viscosity may have a direct bearing on shelf-life performance. Fortunately, this behavior is easily evaluated using inexpensive instrumentation that can perform the tests quickly and repeatedly, thereby assuring the quality customers expect in today’s medicines.