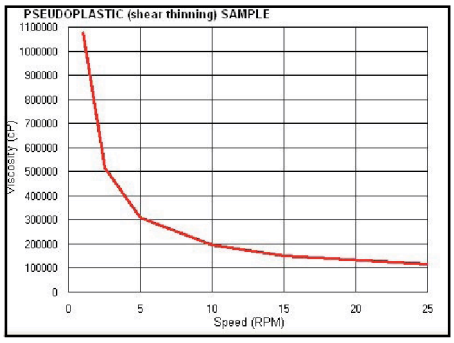
Comprehensive Physical Testing of Pharmaceutical Liquids, Solids and Related Packaging Materals

Pharmaceutical products may be in the form of liquids, ointments or solids, all of which must be packaged. Physical testing on each of these products, and their packaging, is usually done for quality control purposes. Liquids are often tested for viscosity using a Brookfield rotational viscometer. Ointments are tested for yield stress and their shear thinning flow characteristics. Solids, tablets and capsules are tested to determine their hardness using a compression tester.

Testing liquids for viscosity usually involves a test methodology resulting in a single centipoise value. This value is usually compared to a pass/fail scale. Additional viscosity testing should be considered, when establishing the test method, in order to fully characterize rheological properties of non-Newtonian fluids.

Ointments are liquids with the special property of yield stress. For example, most creams and lotions are intended to be thick when standing to prevent them from flowing away from the intended area of use, but they must also flow easily when rubbed so they are easy to apply. This rapid thinning property is termed "pseudoplasticity", but that simply means the ointment is easy to spread due to its rapid loss of viscosity when made to flow during while rubbing (see figure 1).

Figure 1 / Pseudoplastic (shear thinning) sample graph



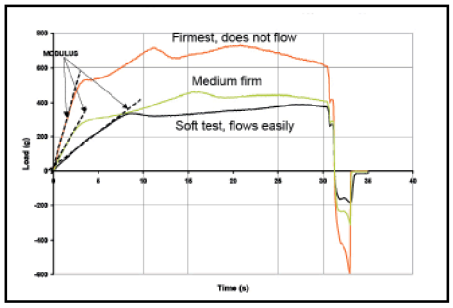
Shear rate is a term used to describe the rate of flow of a fluid and is expressed in units of inverse seconds (s-1). The graph shows only RPM, but shear rate and RPM are directly related. Shear rates from 0 s-1 to 1 s-1 describe a nearly motionless fluid. The action of rubbing lotions and ointments into the skin can easily result in shear rates of over 100 s-1 and may even be as high as 10,000 s-1. Many products are formulated to perform exactly this way.

While viscosity and yield stress are usually measured with a viscometer or rheometer, a Texture Analyzer can also be used for QC testing of these products. A test is conducted by driving a cylindrical probe slowly into the product while measuring the resulting force (see figure 2).

Figure 2 / Extrusion Cell Fixture allows backward or forward extrusion

The properties of viscosity and yield stress will result in unique load profiles during probe descent. The increase in positive force recorded just after the probe contacts the sample surface is an indicator of stiffness, or modulus. In Figure 3 this slope is indicated by the dotted lines labeled "modulus".

Figure 3 / Texture Profile Comparison of different types of ointment



As the probe descends and displaces the sample, the combination of stiffness (yield stress) and flow-ability (viscosity) contribute to the force profile. The shallower slope and lower, flatter force plateau of sample one is caused by its lower yield stress and viscosity. It will flow more readily than the other samples. Then, as the probe withdraws, a negative load is encountered because the ointment adheres to the probe. These force profiles become the primary test result.

Samples can be compared, and quality control can be assured, by repeating the same test in successive products and comparing results. A manufacturer might use this information to adjust the formulation until the force profiles compare favorably to that of an established, acceptable product. Test considerations which affect results of a texture analysis test include:

1) Sample temperature
2) Dimensions of sample container
3) Dimensions of test probe
4) Surface of the sample must be flat and level

5) Homogeneity; sample is smooth with no entrapped air
6) Probe travel speed and penetration distance

Each of the test techniques described above can provide information about one or more of the physical properties of lotions and ointments. When used in combination, these techniques will compliment and reinforce each other.

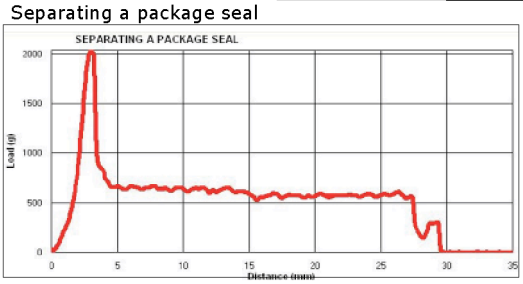
Mechanical properties of solid tablets can also be characterized with a texture analyzer. It is necessary to use the proper fixtures needed to hold your tablets or capsules in place. Puncturing gelatin capsules, crushing tablets or shearing multi-compound tablets can all provide insight into the physical properties of such pharmaceutical products.

Testing of packaging includes puncturing blister packs, ensuring the integrity of closure seals. Blister packs are simply secured onto a punch table and penetrated with a probe of the tester's choice. The peak load indicates the relative force needed to push the product through its package (see figure 4).

Figure 4 / Grip Samples to imitate "tearing" or pulling motion

Closure seals of flexible packaging require precise sample preparation. Test strips of equal width must be prepared such that the seal is equidistant from either end. The strip is then secured between two grips as shown. The test method pulls the grips apart far enough to separate the seal while monitoring the force required. Detailed analysis of the seal is possible and even small differences can be distinguished. In the graph shown in figure 5, 2kg was required to begin seal separation while the remainder of the seal required a steady 700g of force to open it.

Figure 5 / Separating a package seal



Texture Analyzers can be useful and flexible tools in pharmaceutical quality control. Many different properties can be assessed with a single tool. If you'd like to learn more about any of these applications contact Brookfield Engineering Labs., Inc.

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