Poster 22

Use of ASAP for Accelerated Stability Determinations of Viscosity Degradation in Pharmaceutical Polymers

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Purpose

The molecular weight of water-soluble polymers plays a role in controlling drug release from matrix tablets. Molecular weight changes during shelf life could result in adverse performance resulting in failures with respect to dissolution specification limits. The Accelerated Stability Assessment Program (ASAP) approach is used widely in pharmaceutical modeling of shelf life and packaging. ASAP employs isoconversion (time to hit the specification limit at each condition) with designed temperature/RH conditions (based on a humidity-corrected Arrhenius equation) to build a stability model. This project tests the hypothesis that the ASAP approach can provide a rapid and accurate methodology for modeling molecular weight changes.

Methods

Changes in the molecular weight of water-soluble polymer powders were quantified based on viscosity changes of the materials once dissolved. Samples of high molecular weight hydroxypropyl cellulose (HPC) powder (550 mg) were weighed into glass vials and set up in canning jars (n=3 samples) with varying saturated salt solutions to control humidity (2 – 50% RH). Canning jars were placed in 50, 60, 70, and 80°C ovens for stressing up to 21 days, with all conditions designed to be below the glass transition temperature (Tg) of the polymer. Control samples were stored at 5°C. Stressed and control samples were re-equilibrated to ambient conditions for 48 hours prior to measurement. Aqueous solutions (1% w/w) were prepared from the equilibrated powder. These solutions were stirred for 48 hours and tested in an AMETEK® Brookfield DV2T viscometer using the Small Sample Adapter at 60 rpm and 25°C.

Results

The viscosity decreases for stressed samples of the polymer, consistent with loss of molecular weight as the polymer ages. A mathematical model based on the viscosity data (using ASAPprime® software) shows that the isoconversion times fit well the modified Arrhenius equation (R2 = 0.96) with the behavior showing primarily temperature sensitivity (activation energy), with little humidity dependence (low B term).

Conclusion

A viscosity sample preparation method was developed, and an ASAP study was designed to generate viscosity changes in a water-soluble polymer. The observed experimental viscosity decrease was well modeled by the ASAPprime® software.

Keywords: Accelerated Stability Modeling, Viscosity