Stability Study of the Sol/Gel Reversible Phase Transition of a Temperature-Responsive Hydrogel

Temperature-responsive hydrogels are a class of polymers. They form by binding water to the hydrophilic groups of the polymer via hydrogen bonds. At lower temperatures this bond is stable but will gradually break with increasing temperature. Temperature-responsive hydrogels have attracted increasing attention and have been widely studied for their specific structures and smartly tuneable properties. The excellent temperature-responsive performance and reversible reciprocity are highly valued in various applications, such as drug release, pesticide release, cell culturing, protein purification, industrial coatings, sensors, etc. It is of great significance to study the Sol/Gel reversible phase transition behaviour and destabilisation mechanisms. A study of the temperature reversibility and phase transition of pharmaceutical hydrogel, using the MultiScan MS 20 (Fig. 2) from DataPhysics Instruments, is being presented throughout this application note.

Fig. 1: Pharmaceutical hydrogel that shows a perfect temperature reversibility between 20 °C and 50 °C.

Keywords: MultiScan 20 ▪ Stability Analysis ▪ Temperature Response & Reversibility ▪ Hydrogel ▪ Phase Transition

Technique and Method

The MultiScan MS 20 (Fig. 2) from DataPhysics Instruments is the measuring device for an automatic optical stability and aging analysis of liquid dispersions and the comprehensive characterisation of time- and temperature-dependent destabilisation mechanisms. It consists of a base unit and up to six connected ScanTowers with temperature-controlled sample chambers. The ScanTowers of the MS 20 can be individually controlled and operated **at different temperatures (4 °C to 80 °C)**.

With its matching software MSC, the MS 20 is an ideal partner for the stability analysis since **even the slightest changes** within dispersions can be detected and evaluated. The MS 20 enables a fast and objective analysis of the dispersion stability as well as conclusions on possible **destabilisation mechanisms**.

Fig. 2: DataPhysics Instruments stability analysis system MultiScan MS 20 with six independent ScanTower.

Experiment

20 g of a pharmaceutical hydrogel, whose storage temperature is room temperature, was poured in a transparent glass vial. To ensure that there are no air bubbles in the gel, the sample vials were vibrated gently using an ultrasonic bath and settled for 2 hours at room temperature before measuring.

During the temperature reversibility measurement, the temperature was increased from 20 °C to 50 °C and then decreased from 50 °C to 20 °C using a ramp of 6 °C/h. Additionally, the sample was kept at a constant 20 °C for 6 h and at a constant 50 °C for 10 min during each cycle. The temperature cycle was repeated three times and the samples were scanned every 15 min for a total duration of 36 h. The measured zone is between 0 mm (bottom of the vial) and 57 mm (fill level of the vial). A second experiment was conducted at T = 50 °C with scans every 5 min for 22 h, in order to study the destabilisation mechanism at high temperatures. Fig. 1 shows the sample vial at the end of the measurement at 20 °C and at 50 °C, respectively.

Results

1. Temperature reversibility

Fig. 3 shows the transmission intensities against the position in the hydrogel sample. The colour-coding of the curves indicates the time at which they were recorded, from red (start of the experiment, t = 0 s) to purple (end of the experiment, t = 36 h). The transmission diagram shows a clearly time-dependent as well as position-dependent change of the signal in the top layer between 30 mm and 39 mm, which can be evaluated using the “values method” in the MSC software.

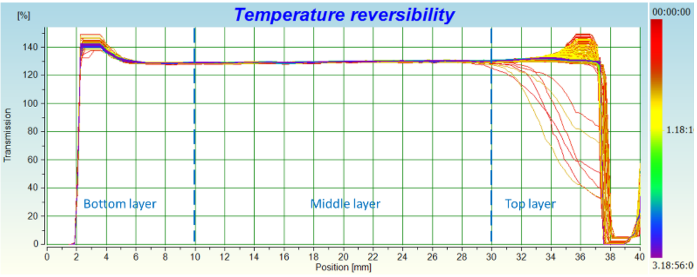

Fig. 3: Transmission intensity diagram of hydrogel.

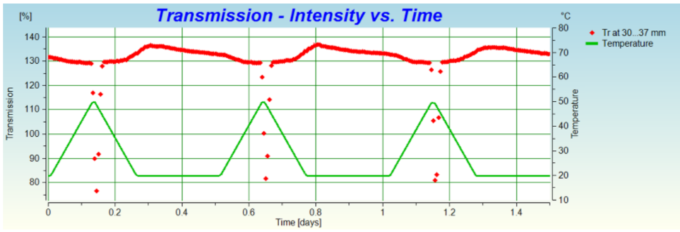

Fig. 4: Changes in transmission intensity of gel over time (red) and corresponding temperature diagram (green).

The changes in transmission intensity (red) and the test temperature (green) over time are shown in Fig. 4. The transmission intensity is relatively constant between 20 °C and 45 °C, indicating that the stability of the hydrogel is very high in this temperature range. However, the transmission drops dramatically when the temperature reaches around 50 °C, indicating that the interaction forces between water and polymer are not strong enough at higher temperatures, leading to a sol–gel system. The transmission values return to the initial values when the temperature is cooled to around 45 °C, revealing that the hydrogen bonds are reformed between polymer and water resulting in a gel system. Notably, the change in transmission is reversible over the temperature cycles. It can be concluded that the hydrogel exhibits a highly sensitive temperature response and excellent temperature reversibility.

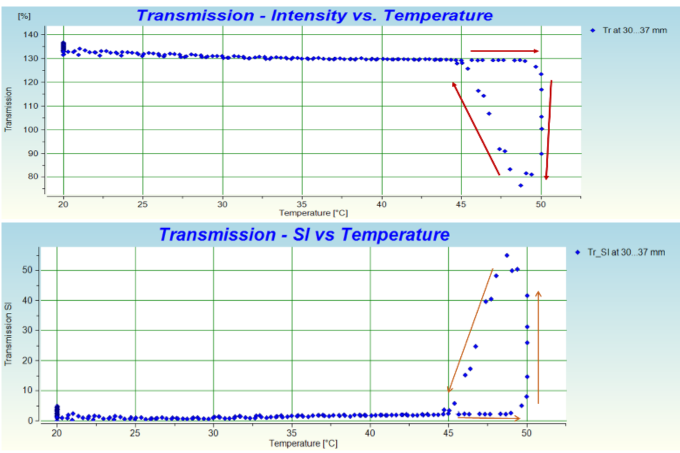

Fig. 5: Changes in transmission intensity & transmission stability index (SI) of the hydrogel vs. temperature.

In consistency with the above results, the changes in transmission intensity and the stability index SI over temperature (Fig. 5) support that the hydrogel has a completely temperature-reversible behaviour between 20 °C and 50 °C.

2. Destabilisation kinetics at 50 °C

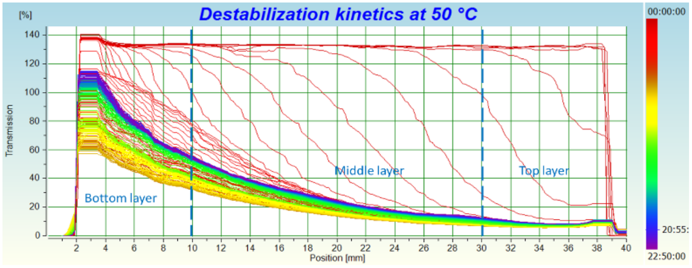

Fig. 6: Transmission intensity diagram of the hydrogel.

To get an insight on the destabilisation mechanism of the gel at high temperatures, the stability over time was studied at 50 °C. Fig. 6 shows that the transmission intensity decreases over time and increases towards the bottom of the vial. This suggests that the hydrogen bonds between water and polymer are broken at high temperatures and water drops coalesce leading to a sol-gel system.

Fig. 7 shows that the transmission decreases rapidly in the first hour with a change rate of 137.9 %/h, indicating that most of the water is drained and the segments of polymers shrink in the first hour. Additionally, a slow increase of the transmission intensity is exhibited after 6 hours, suggesting that the coalescence of drops is predominant.

In consistency with the temperature reversibility test, the top layer is more unstable than other layers.

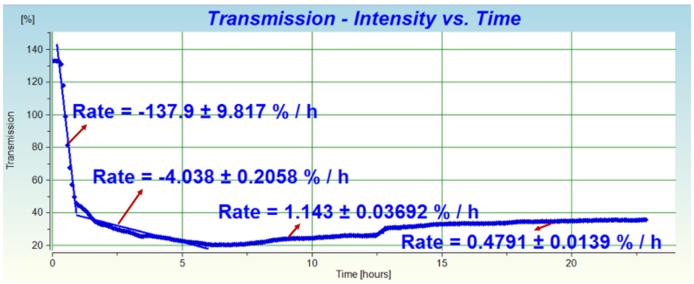

Fig. 7: Transmission intensity (position: 3 – 35 mm) of the hydrogel vs. time.

Summary

Using the MS 20 stability analysis system and its corresponding MSC software, an **easy and fast way** to study the **temperature reversibility**, **phase transition** and **destabilisation mechanisms** of a hydrogel system could be demonstrated. Changes can be detected sensitively and reliably which enables the producer to anticipate and quantify stability issues and thus guarantee time and cost optimal product development.

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