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PolyVivo (AK19) Thermogelation Properties

Purpose

To determine the thermogelation properties of triblock poly(lactic-co-glycolic)-b-poly(ethylene glycol)-b-poly(lactic-co-glycolic) (PLGA-PEG-PLGA) polymer Akina catalogue number AK19.

Rheometry

Preparation: AK19 Batch #1 dissolved in distilled water as 20% (w/v) solution. Another solution was prepared by dissolving AK19 Batch#1 and 1000 Da Polyethylene glycol (Carbowax 1000) to concentrations of 20% and 5.1% w/v respectively in the same solution. Dissolution of each solution was done over a period of a few days at 4°C. Control solutions of distilled water and 30% Pluronic® F127 were also made to represent a known non-thermogel and known thermogel respectively.

Rheometry: Viscosity and Sol-Gel curve was determined via rheometry using an AR550 (TA instruments) rheometer. This Rheometer was equipped with a 60 mm cone 2° top plate with a heat break and 62 µm truncation, a peltier temperature controlled bottom plate with a heat-sink water supply maintained at 20°C by an RTE thermo-chiller/circulator pumping a ~10% ethylene glycol solution through the plate. The bottom plate had an initial temperature setting of 4°C and approximately 2 ml of each chilled solution to be tested was placed in between the cone and plate with an initial distance of 100 µm. Capillary force drew the sample into the gap between the plates and then the top plate was lowered to its truncation gap of 62µm. The front of the rheometer was covered lightly with Glad ware press and seal wrap to reduce evaporation.

Viscosity: Initially the test solution was equilibrated to 5°C for one minute and then run through a step flow program. This program ramped the shear rate from 1 to 20 (1/sec) with 5 points per decade and a constant time of 10 seconds with an averaging of the last 5 seconds. Table 1 indicates the viscosity of each solution in mPas at a shear rate of 10/sec.

Table 1. Viscosity of sample solutions at 5°C

Sample AK12 Solution	Viscosity (mPas) (10/sec)
DI water	2.150
20% AK19 B#1 w/v in DI water	5.803
20% AK19 B#1 + 5% PEG1000 w/v in DI water	9.322
30% w/v Pluronic F127 in DI water	58.99

As can be seen the cold-water viscosity of the polymer solutions was on the same order of magnitude as DI water and can flow easily.

Sol-Gel

The rheometer was set to run a temperature sweep with the conditions as shown in Table 2.

Table 2. Rheometer temperature sweep conditions

Item	Setting	Item	Setting
Initial temperature	5°C	Control Variable	0.1% Strain
Sweep Range	5°C-40°C	Frequency	Single-6.283 rad/s
Increment	2.5°C	Conditioning Time	3 seconds
Equib. Time	3 Minutes	Measurement Time	3 seconds

The oscillation curve was obtained with G' (Pa), G'' (Pa), and delta (degrees) displayed (Fig 1-4). In the following image series G' is shown as a red line, G'' is shown as a blue line, and delta is shown as a black line. Note a decrease in delta or increase in G'/G'' indicates the solution becoming solid/viscous. In this case a drastic increase in G'' indicates a very viscous solution.

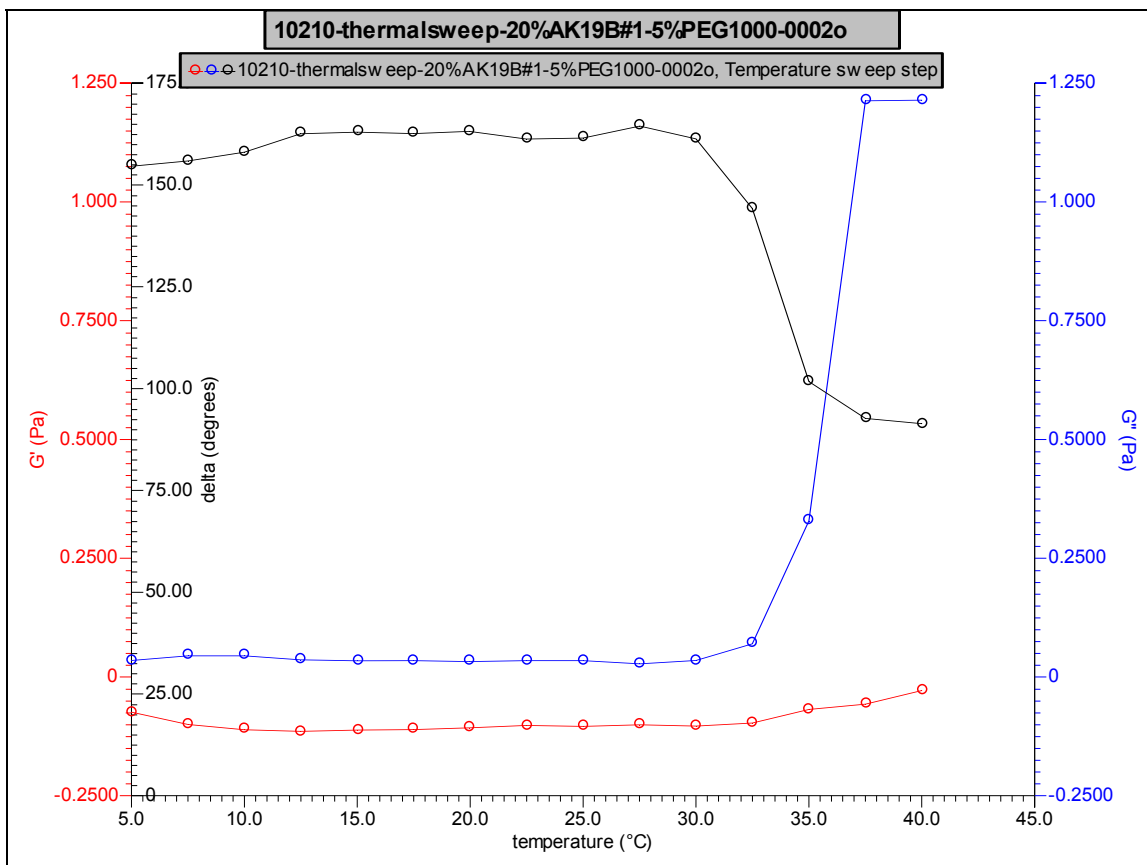


Figure 1. Rheometry Curve from 20% (w/v) AK19 B#1+ 5% PEG1000.

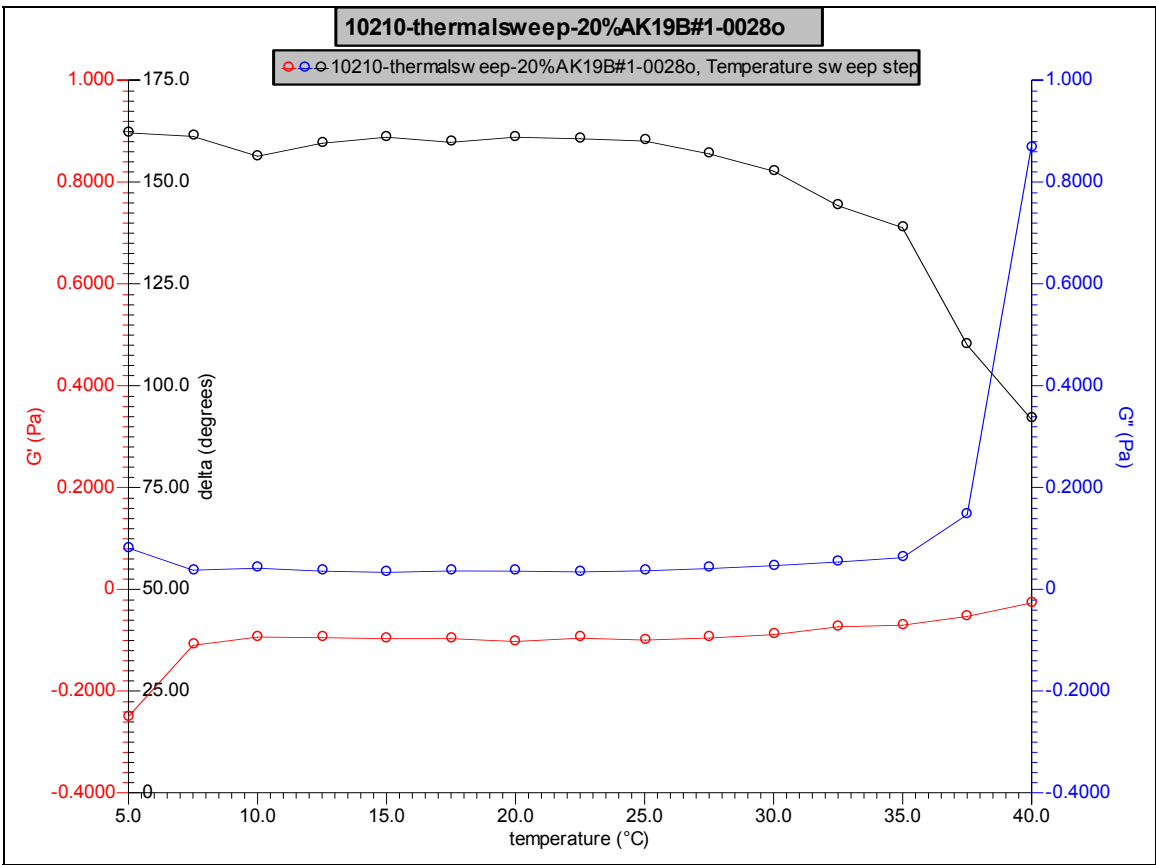


Figure 2. Rheometry Curve from 20% (w/v) AK19 B#1

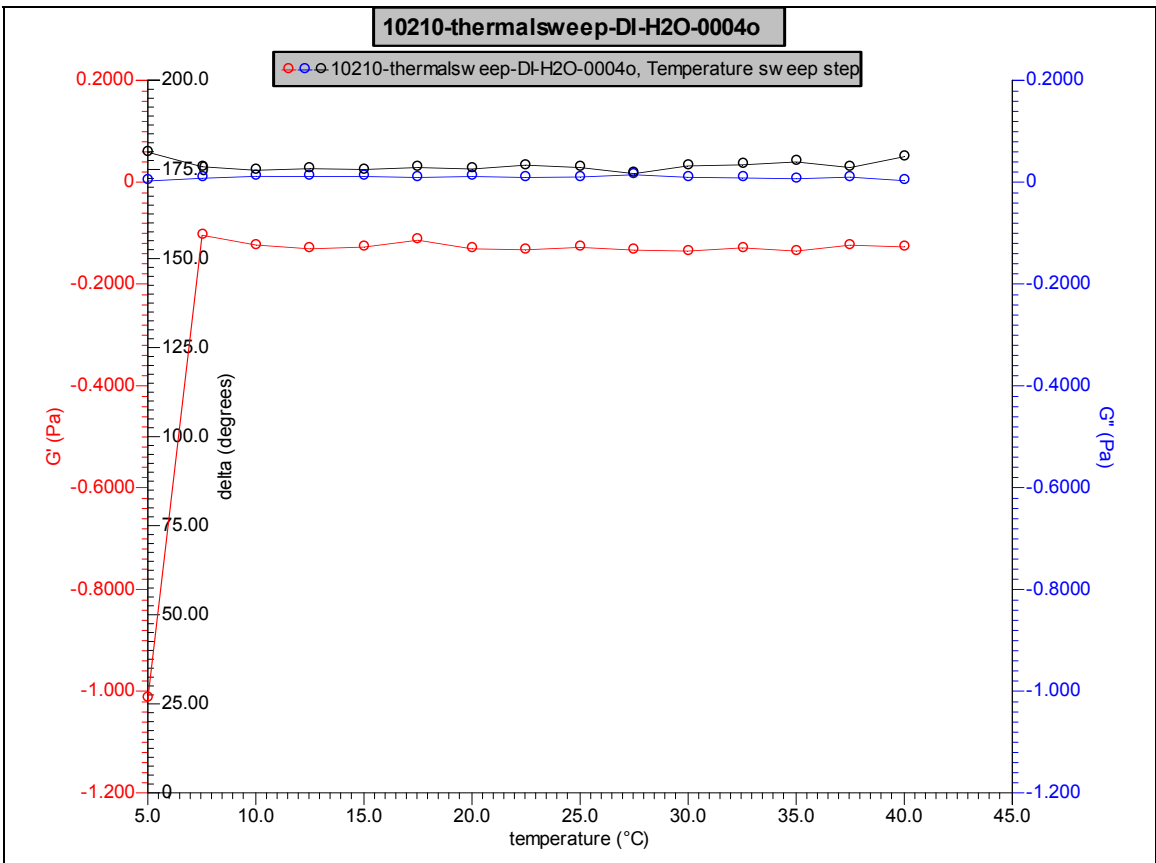


Figure 3. Rheometry Curve from DI H2O

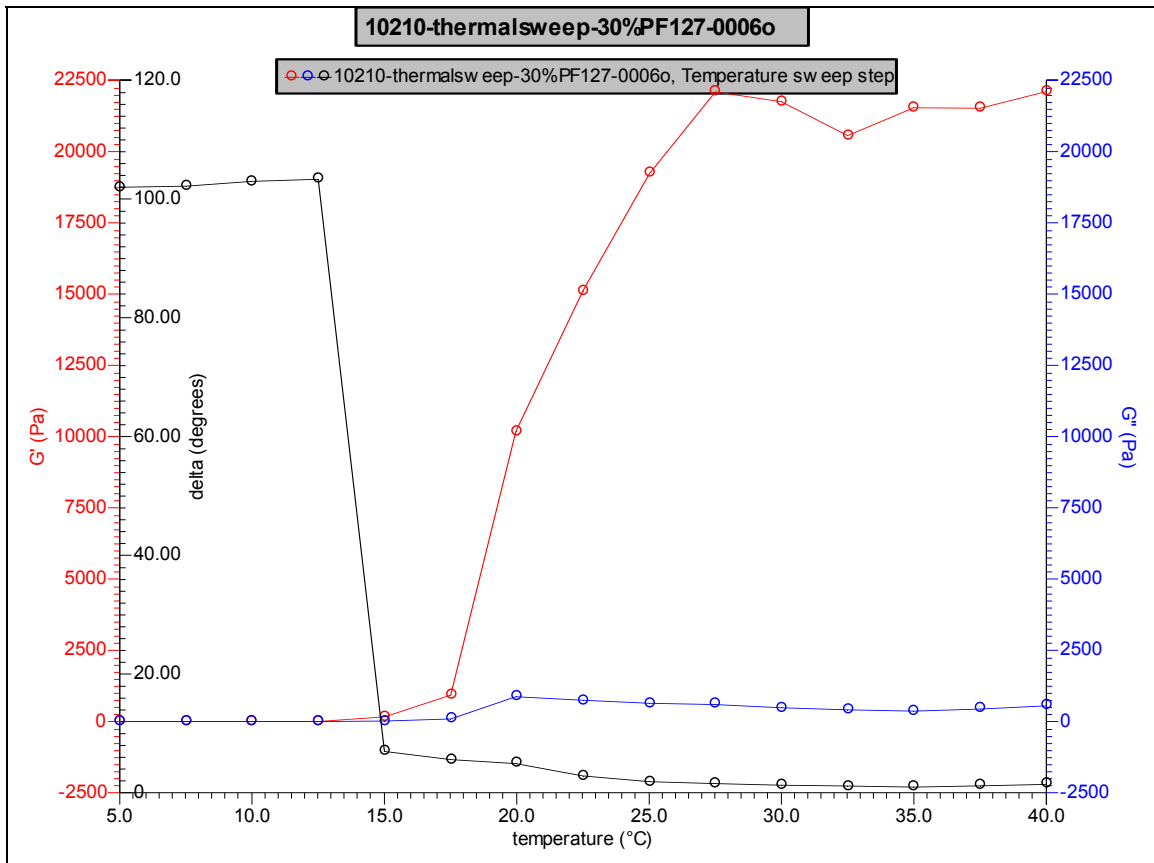


Figure 4. Rheometry Curve from 30% Pluronic F127 (known thermogel)

As can be seen the controls behaved as expected. DI H₂O is not impacted by changing temperature, Pluronic displays a clear transition between 15-20°C to a more gelled form. Polyvivo AK19 (20%) by itself has a weak increase in viscosity beginning around 35-40°C, but when in the presence of PEG1000 this transition decreases to 30-35°C indicating that the thermogelling properties can be affected by additives.

Conclusion

Polymer AK19 (PLGA-PEG-PLGA) is a thermosensitive polymer with a transition to a more viscous form at 20% w/v concentration. The transition temperature is slightly higher than the useful range, however combinations with other materials may reduce the transition temperature to a more useful level.