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Thermo-Gelation Properties AK12 Batch 1 in Different Solution Conditions

Purpose

To further the understanding of rheological and thermogelation properties of triblock poly(lactic-co-glycolic)-b-poly(ethylene glycol)-b- poly(lactic-co-glycolic) (PLGA-PEG-PLGA) polymer Akina catalogue number AK12 in different solvent conditions.

Methods

Solution Preparation

Polyvivo AK12 is a low molecular weight thermosensitive triblock copolymer. In solid form it is gelatinous at room temperature yet flows relatively easily when gently warmed to 37°C. A portion of this polymer was warmed and transferred into a series of 4 ml vials by pouring into the tared vial. To the first three vials a calculated amount of distilled water was added to form 10, 20, and 30% w/v solutions respectively. The next two vials had a fixed amount of 20% w/v AK12 utilized. The first of these vials had phosphate buffered saline (PBS) + 0.02% sodium azide used to dissolve the AK12 while the second one had PBS+0.02% Azide and had human serum albumin (HSA) added to a total concentration of 1% w/v. All of these vials were mixed for several days at 4°C.

Rheometry

Viscosity and Sol-Gel curve was determined via rheometry using an AR550 (TA instruments) Rheometer. This Rheometer was equipped with a 60 mm 2° top plate, 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 solution to be tested was placed in the middle of the bottom plate. The top plate was lowered to a preset gap 62 µm. Capillary force drew the sample into the gap between the plates and the sample was visually checked for proper loading. The rheometer was set to run both a viscosity test and a temperature sweep. The viscosity test was performed at a constant 5°C. After equilibrating the solution for 1 minute, a stepped flow program was run from shear rates of 1 to 20 (1/sec) with 5 points per decade and with a constant time of 10 seconds with the average of the last 5 seconds used for the measurement. Following this the solution was held at a constant rate of 10 (1/sec) for 1 minute

with measurements every 10 seconds. The conditions used for the subsequent temperature sweep are shown in Table 1.

Table 1. 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

Results

Viscosity

An example of the step flow and the peak hold step is shown in Figure 1. As can be seen, the graph is fairly stable in terms of viscosity around the 10 (1/sec) range indicating that there are no inertia affects or specific shear effects occurring in this region. The viscosity was calculated from the average of the 6 measurements during the peak hold step and is shown in Table 2 with ± standard deviation.

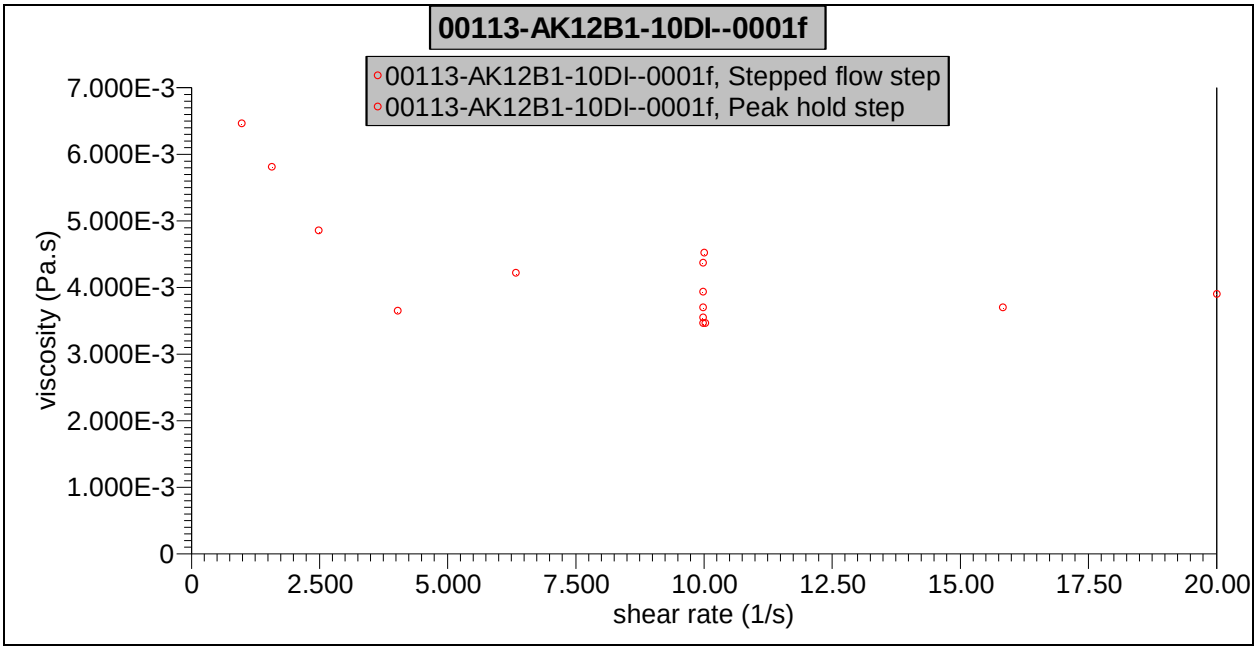


Figure 1. Example viscosity step and peak hold

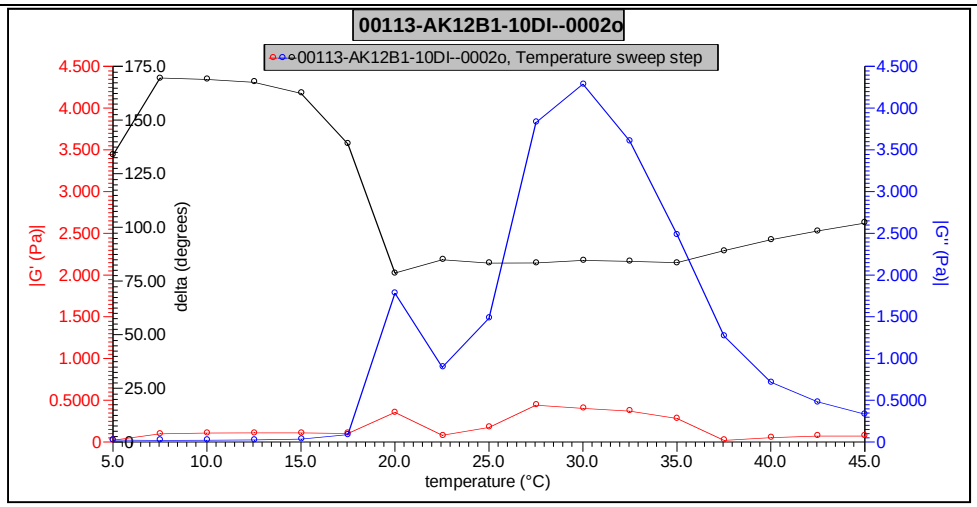
Table 2. Viscosity of sample AK12 solutions at 5°C

Sample AK12 Solution	Viscosity (mPas) ± SD
10% w/v in DI water	3.87 ± 0.43
20% w/v in DI water	13.07 ± 1.65
30% w/v in DI water	42.70 ± 1.44
20% w/v in PBS	11.77 ± 0.82
20% w/v in PBS + 1% HSA	12.61 ± 1.13

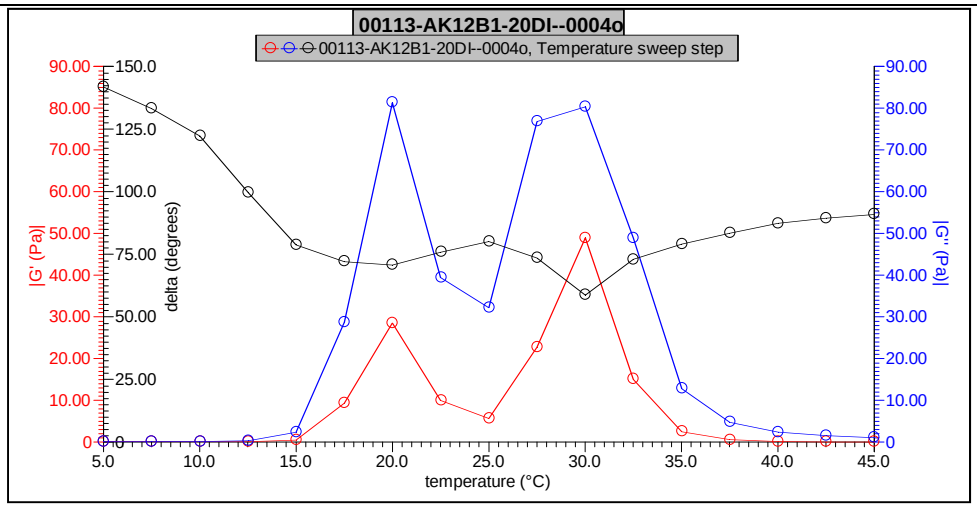
The viscosity of these solutions is all fairly low at these temperatures. For example: pure water at 20°C has a viscosity of 1 mPas, human blood has a viscosity of 3-4 mPas (37°C) and pure olive oil has a viscosity of 81 mPas (http://en.wikipedia.org/wiki/Viscosity). These results indicate that for a suggested solution of 20% w/v the cold viscosity is only slightly higher than that of human blood and well below that of light oils. The presence of PBS and/or albumin protein has no substantial impact on the viscosity.

Sol-Gel

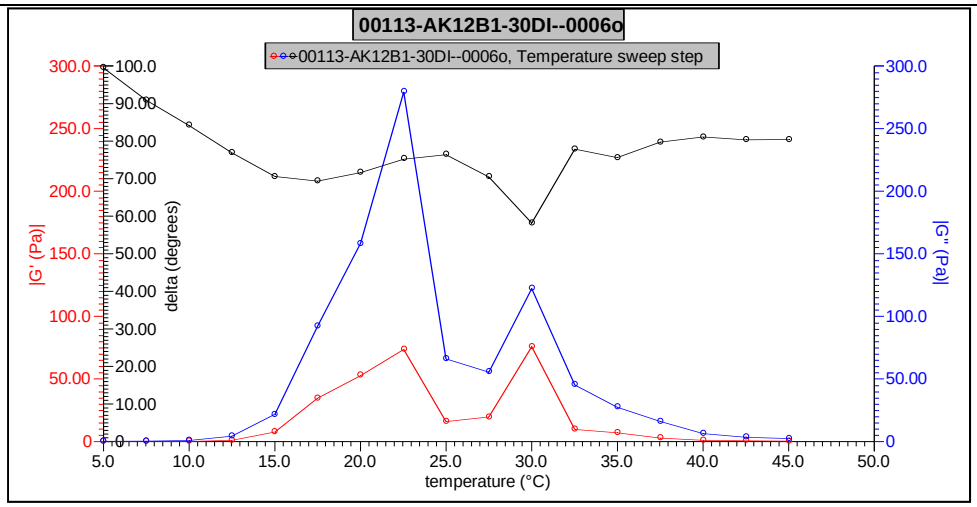
The oscillation curves were obtained with G'(Pa), G" (Pa), and delta (degrees) displayed (Fig 2). In the image series G' is shown as a red line, G" is shown as a blue line, and delta is shown as a black line. Note a decrease in delta or increase in G'/G" indicates the solution becoming solid/viscous. At higher temperatures the gel releases water and precipitates back to solid form.



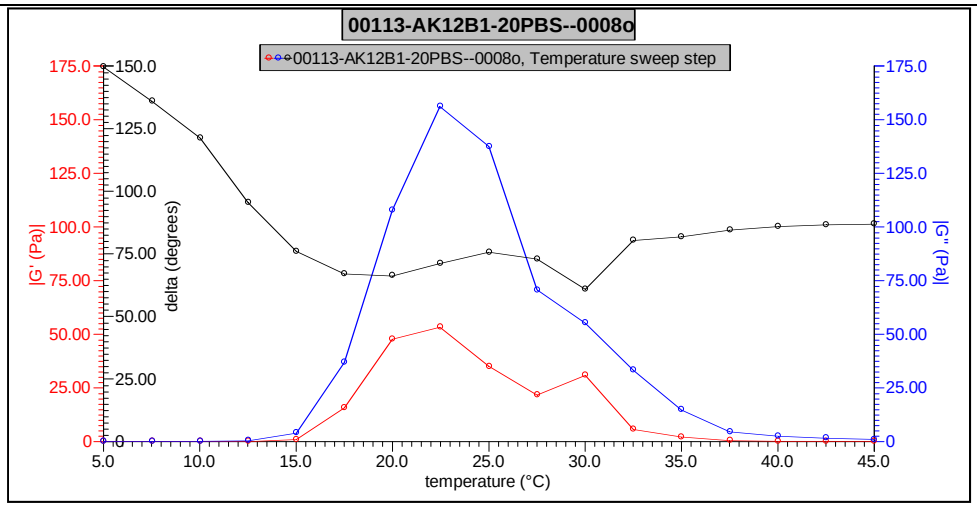
A. 10% w/v in DI water



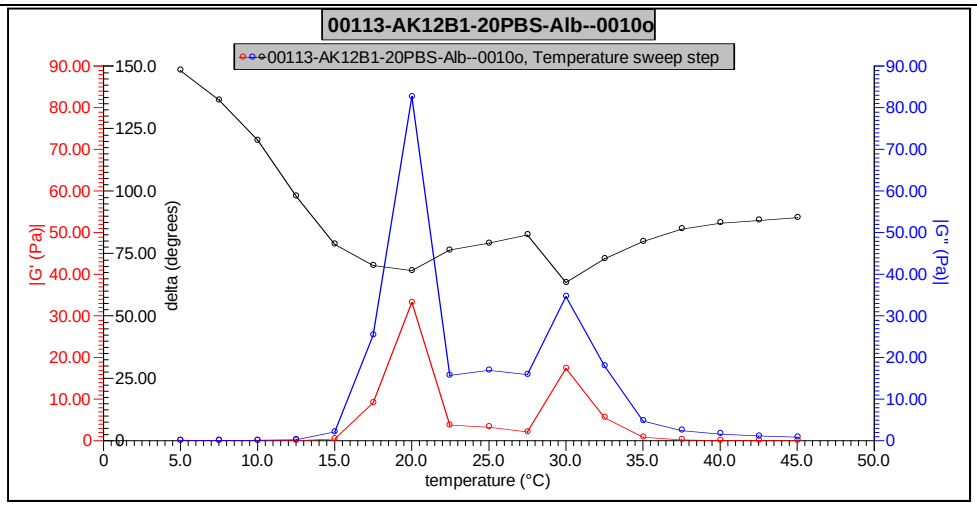
B. 20% w/v in DI water



C. 30% w/v in DI water



D. 20% w/v in PBS



E. 20% w/v in PBS + 1% HSA

Figure 2. Temperature sweep data for AK12 in indicated solvent conditions.

Conclusion

All of these polymer solutions have a thermal behavior which impacts their rheological properties between 5-37°C thus indicating that AK12 has thermo-sensitive properties.