Poster Number M0632

# Assay of Polymeric Sustained Delivery Systems for Carrier Properties

J. Garner[1], S. Skidmore[1], K. Park[1], H. Park[1], S. Choi[2], Y. Wang[2]

[1]Akina, Inc., West Lafayette, IN 47906 USA, [2]Food and Drug Administration, Silver Spring, MD 20993, USA

2016 AAPS ANNUAL MEETING AND EXPOSITION
NOVEMBER 13–17, 2016
COLORADO CONVENTION CENTER, DENVER
aaps

## PURPOSE

- Establish a testing protocol for characterization of poly(lactide-co-glycolide) (PLGA) used in injectable long-acting depot formulations.
- Allow for examination of the qualitative and quantitative (Q1/Q2) sameness between the reference and generic products.
- Parameters are the molecular weight, lactide:glycolide (L:G) ratio, and endcap group of PLGA polymers.

## METHOD

- Commercially purchased Risperdal® Consta®, Trelstar® 3.75, 11.25, and 22.5 mg doses, and Sandostatin LAR® were dissolved in dichloromethane (DCM) (**Fig. 1**).
- Solutions filtered and dialyzed for three days (MWCO 6000-8000 Da) against an organic solvent.
- Precipitated in a stirring excess of hexane and dried under deep vacuum.
- The polymer component was then analyzed by gel permeation chromatography (GPC) (**Fig. 2**), $^{1}$H nuclear magnetic resonance (NMR) and $^{13}$C NMR (**Fig. 3**). (1)


Figure 1. Dissolution of microparticles

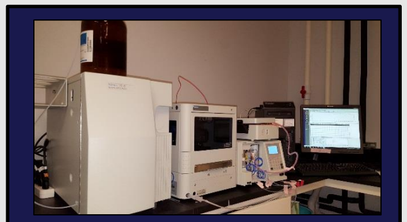

Figure 2. Waters Breeze 2 GPC system

Figure 3. NMR system Bruker AV-III-500HD[2]

## RESULTS

- GPC chromatographic data used to determine apparent weight average and number average molecular weights (**Figure 5**). No noticeable differences in the chromatograms were observed for Sandostatin LAR® as compared to other PLGAs.
- The LA:GA ratio was determined by relative peak integration at 5.2 ppm (LA, 1H) and 4.8 ppm (GA, 2H), respectively (**Figure 6 A, B**).
- $^{13}$C NMR was performed using a cryoprobe for a total of 12,000 scans acquired over 12.5 hours to maximize signal/noise ratio. Ester end-capped PLGA could be observed by a peak at 14 ppm in $^{13}$C NMR. No discrete peaks were observed for glucose (**Figure 6 C**).
- **Table 1** displays parameter values for clinical products assayed.

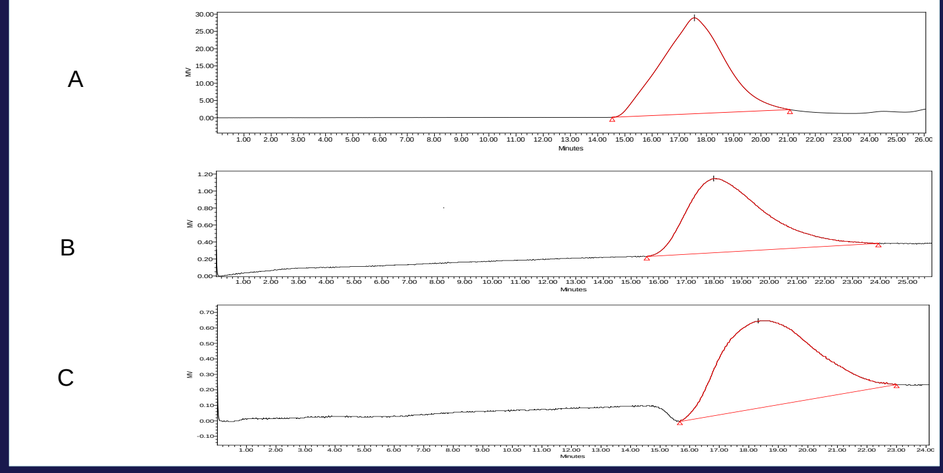


Figure 5. Chromatograms (GPC) Risperdal Consta (A), Trelstar 11.25 mg (B), and Sandostatin LAR (C) .

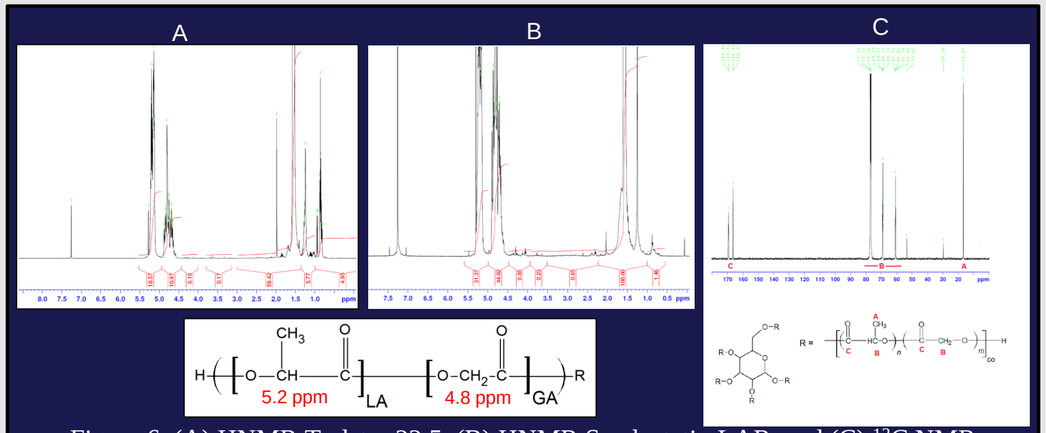


Figure 6. (A) HNMR Trelstar 22.5, (B) HNMR Sandostatin LAR, and (C) $^{13}$C NMR Sandostatin with peak assignments.

Table 1. Assayed PLGA parameters of designated clinical products.

| Formulation | L:G ratio (molar) | $M_n$ | $M_w$ | Endcap |
|---|---|---|---|---|
| Risperdal Consta | 78:22 | 44,875 | 111,142 | Ester |
| Trelstar (3.75 mg) | 52:48 | 25,192 | 85,207 | Ester |
| Trelstar (11.25 mg) | 74:26 | 47,214 | 72,286 | Acid |
| Trelstar (22.5 mg) | 77:23 | 46,368 | 74,042 | N/A |
| Sandostatin LAR | 58:42 | 24,549 | 49,421 | N/A |

## CONCLUSION

- The molecular properties of PLGAs in three clinical products were determined.
- Trelstar 22.5 mg appears to have similar PLGA as the 11.25 mg, however, it has double the duration (6 months vs 3 months) indicating that this product is likely a combination of two types of PLGA and the assays are revealing the average of the two types.
- According to product labeling, Sandostatin LAR is made of glucose-star PLGA.
- The techniques applied including conventional GPC with refractive index detection, HNMR, and $^{13}$C NMR do not elucidate any details regarding end-capping, star-structure, or degree of branching.
- There is a need for advanced assay techniques to define parameters of mixed PLGAs and star/branched PLGAs.

## ACKNOWLEDGEMENTS AND REFERENCES

**Acknowledgement:** This work is supported by Grant U01FD05168 from the Food and Drug Administration (FDA, Center for Drug Evaluation Research (CDER), Office of Generic Drugs (OGD). This article reflects the views of the authors and should not be construed to represent FDA's views or policies.

**References:**

**1.** Garner, John, et al. "A protocol for assay of poly (lactide-co-glycolide) in clinical products." *Int. J. Pharm.* 495 (2015): 87-92.

**2.** http://www.pinmrf.purdue.edu/instruments/av500.shtml