Effect of Polymer Source Variation on Physicochemical Properties of Risperidone Microspheres

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PURPOSE

- Poly(lactic-co-glycolic acid) (PLGA) is inherently heterogeneous and challenging to ensure Q1 (qualitative) sameness.
- Differences in the physicochemical properties of PLGAs from different sources may exist due to variations in the manufacturing process as well as differences in the characterization methods used.
- The purpose of the present work was to investigate the impact of PLGA source variations on critical quality attributes of PLGA microspheres.

MATERIALS AND METHODS

- Risperidone (model drug) was purchased from AK Scientific, Inc. Three PLGA polymers with similar inherent viscosity (IV), lactic acid to glycolic acid (L/G) ratio, and end groups as that used in the commercial product Risperdal Consta®, were purchased from three different vendors.
- Various physicochemical properties (*e.g.*, IV, molecular weight (Mw), polydispersity index (PDI), L/G ratio, glass transition temperature (Tg), *etc.)* of the three different polymers were characterized.
- Three microsphere formulations were prepared *via* a solvent evaporation method using these PLGA polymers. (Formulation 1 was prepared using polymer 1, *etc*.)
- Various critical physicochemical properties (*e.g.*, drug loading, particle size and porosity*)* of the prepared microspheres were characterized. (Span value = (D90-D10)/D50).

RESULTS

1. Physicochemical properties of polymers from different sources

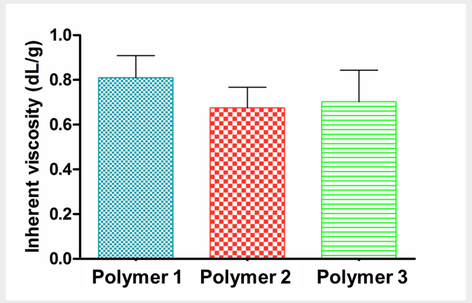

Figure 1: Observed inherent viscosity (*p* value> 0.05) of the PLGA polymers from different sources. All values are expressed as mean ± SD (n=3).

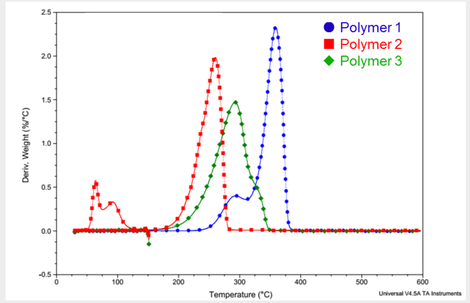

Figure 2: Thermal degradation profiles of the PLGA polymers from different sources.

Table 1: L/G ratio, monomer residue, Mw, PDI and Tg of the PLGA polymers from different sources.

	Reported L/G ratio (%)	Observed L/G ratio (%)	Reported monomer residue (%)	Observed monomer residue (%)	Observed MW (kDa) *	Observed PDI *	Tg(° C) *
Polymer 1	76/24	77.34/22.66	<0.2	0.05	69.72±3.08	1.39±0.02	50.55±0.31
Polymer 2	74/26	72.34/27.66	NA	0.52	85.17±2.00	1.51±0.05	48.30±1.05
Polymer 3	76/24	78.69/21.31	1.1	1.54	81.58±0.65	1.42±0.02	47.01±0.20

* All values are expressed as mean ± SD (n=3).

- PLGA polymers, from different sources, have different Mw and PDI even with similar inherent viscosity;
- PLGA polymers, from different sources, show different thermal properties (Tg, onset temperature).

2. Physicochemical properties of the prepared PLGA microsphere formulations

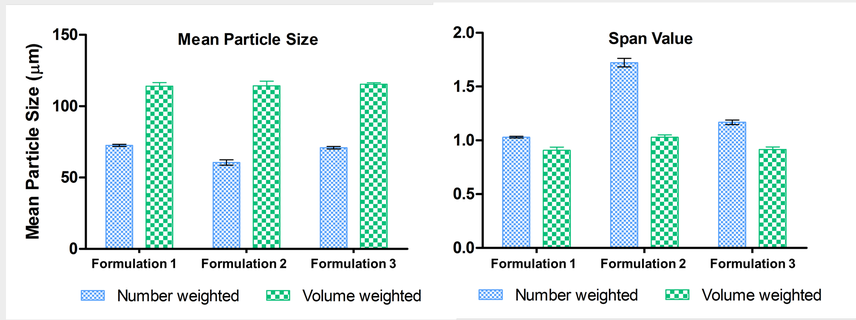

Figure 3: Mean particle size and span values of the PLGA polymers from different sources. All values are expressed as mean ± SD (n=3).

- Formulation 2 has lower mean particle size (population range) which indicates more small particles and thus larger span value compared to formulations 1 and 3

Table 2: Drug loading, porosity and average pore diameter of the prepared formulations

	Drug loading (%,w/w) *	Porosity (%)	Average pore diameter (nm)
Formulation 1	40.98±0.06	62.64	92.09
Formulation 2	45.05±0.61	70.96	159.85
Formulation 3	42.37±1.98	61.71	107.26

* All values are expressed as mean ± SD (n=3).

- Formulation 2 has the largest porosity and pore size .

CONCLUSIONS

- Similar PLGA products with respect to their certificate of analyses showed different physicochemical properties (Mw, PDI, Tg, L/G ratio etc.) from different sources.
- Critical quality attributes (particle size, span value and porosity, etc.) of prepared microsphere formulations using polymers from different sources were determined to be different.

ACKNOWLEDGEMENT

- Funding for this project was made possible by the Food and Drug Administration through the award HHSF223201810115C. The view expressed in this poster are those of authors and do not reflect the official policies of the U.S. Food and Drug Administration.

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