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Impact of Polymer Source Variation on Risperidone Microsphere Performance

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PURPOSE

◆ Determining the qualitative sameness of poly (lactic-co-glycolic acid) (PLGA) has been challenging due to its inherent heterogeneity. Accordingly, performance variation of PLGA-based microsphere drug products (due to altered PLGA characteristics) has been recognized as a critical limiting factor for product development.

✓ The objective of the present study was to: investigate the impact of PLGA source variations on critical quality attributes and release characteristics of microsphere formulations.

METHODS

1. Characterization of Raw PLGA Polymers

Physicochemical Properties	Method of Determination
Inherent viscosity	Viscometer
Molecular weight	Gel permeation chromatography
Monomer ratio (L/G)	Nuclear magnetic resonance
Blockiness (Rc)	

2. Evaluation of Critical Quality Attributes

Critical Quality Attributes	Method of Determination
Drug loading	High performance liquid chromatography
Mean particle size	Accusizer auto dilution particle sizing system
Mean pore size	Mercury porosimetry

3. *In Vitro* Release Testing (USP IV)

	Method of Determination
Medium	10 mM, HEPES buffer with 0.02 % (w/v) sodium azide, pH 7.4
Temperature	37 °C
Flow Rate	8mL/min

RESULTS

1. Characterization of Raw PLGA Polymers

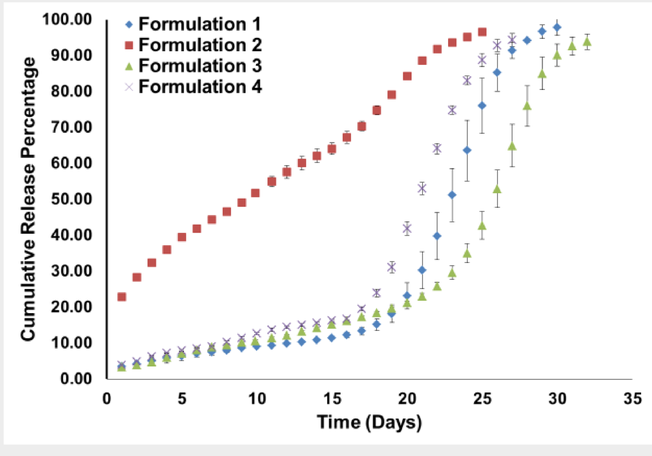
	Reported inherent viscosity (dL/g)	Observed inherent viscosity (dL/g) *	Reported Mw (kDa)	Observed Mw (kDa) *	Reported L/G ratio (%)	Observed L/G ratio (%)	Rc
Polymer 1	0.69	0.81±0.09	Na	60.97±0.79	76/24	77/23	0.45
Polymer 2	NA	0.68±0.09	104.6	77.24±3.88	74/26	72/28	0.60
Polymer 3	0.69	0.70±0.19	92.8	73.65±0.58	76/24	79/21	0.41
Polymer 4	0.71	0.74±0.05	91	75.89±0.65	74/26	78/22	0.55

2. Physicochemical Properties of Prepared Formulations

	Sample	Drug loading (w/w, %) *	Particle size (population, μm) *	Particle size (volume, μm) *	Average pore diameter (nm)
Polymer 1	**Formulation 1**	40.98±0.06	72.60±0.76	114.04±2.52	92.09
Polymer 2	**Formulation 2**	45.05±0.61	60.57±1.86	114.34±3.17	159.85
Polymer 3	**Formulation 3**	42.37±1.98	70.90±0.88	115.38±1.10	107.26
Polymer 4	**Formulation 4**	42.11±0.67	72.69±1.35	116.12±2.19	117.45

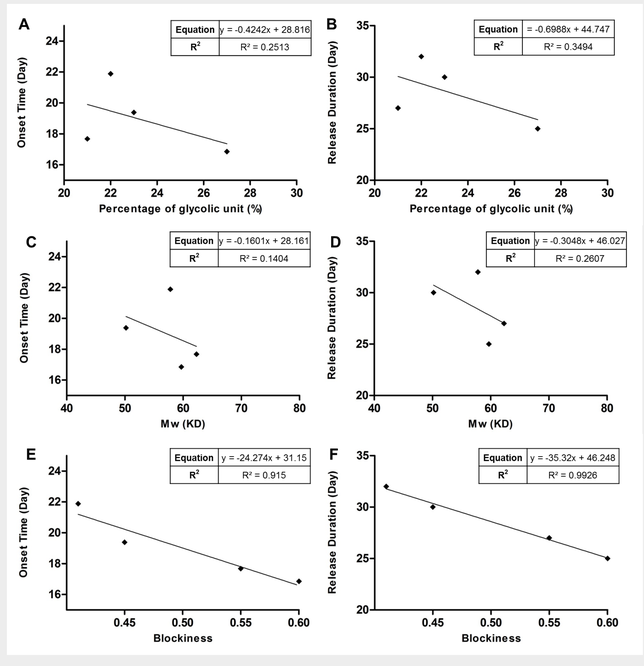
***** The experiments were performed in triplicate and the results are expressed as mean ± SD (n=3).

3. *In Vitro* Release Profile



RESULTS

4. Linear regression of release characteristics (phase transition point, duration) against polymer properties (Mw, L/G ratio, Rc)



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CONCLUSIONS

➢ The PLGAs from different sources had different blockiness. A strong linear correlation was observed between drug release and PLGA blockiness. On the other hand, linear correlation was not observed between drug release and PLGA Mw and/or L/G ratio.

➢ Minor variations such as blockiness should be taken into consideration in PLGA selection for drug product formulation. This work will aid in the establishing additional specifications for PLGA properties that impact drug release.

ACKNOWLEDGEMENT

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