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Stability Tests of Risperidone-Loaded PLGA Microspheres

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PURPOSE

The objectives of the study were

1. To identify critical physicochemical properties affecting PLGA microsphere performance under different storage conditions.
2. To determine whether the developed accelerated *in vitro* release testing method using USP apparatus 4 is capable of detecting changes in the critical physicochemical properties.

METHODS

Preparation of Microspheres: Risperidone PLGA microspheres that are equivalent in formulation composition and components were prepared using different manufacturing processes (*e.g.* solvent systems, and emulsification process).

Storage Stability Testing: The obtained risperidone microspheres (referred to here as Formulations 1 and 2) were stored under different storage conditions as described below:

Table 1. Storage stability testing conditions

Temperature (°C)	Relative Humidity (%)
4	Ambient Humidity
40	Ambient Humidity
40	75 %

Microsphere samples were taken at pre-determined time points (e.g. three months following storage at 4°C/ambient humidity and 8 days following storage at 40°C/ambient humidity and 40°C/75% RH). Physicochemical properties (such as drug loading, particle size, size distribution, polymer molecular weight, morphology, as well as moisture content) of the storage stability testing samples were monitored.

Accelerated *In Vitro* Release Testing: The developed accelerated USP apparatus 4 method[1] was used to investigate the *in vitro* release profiles of the storage stability testing samples. Briefly, approximately 10 mg of microspheres mixed with glass beads were put into flow through cells.

- Release Media – 10 mM Phosphate Buffer, pH 7.4
- Testing Temperature – 45°C
- Flow Rate – 8 ml/min

RESULTS

Real-time storage stability testing results (*i.e.* 4°C/ambient humidity/6 months):

Table 2. Critical physicochemical properties of storage stability samples

Formulation	Time Point	Drug Loading (%)	Volume Distribution	Moisture Content (%)
Formulation 1	Day 0	37.25±0.79	101.01±1.65	0.07
	Month 6	37.01±0.04	102.97±4.64	0.37
Formulation 2	Day 0	35.59±0.11	108.67±6.65	0.13
	Month 6	35.35±0.24	128.95±3.21	0.17

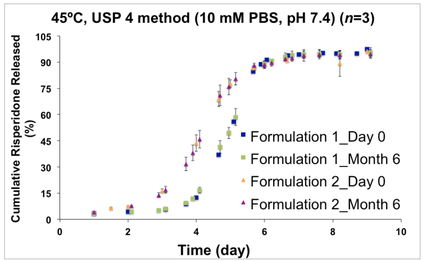

Figure 1. Comparison of *in vitro* release profiles of real-time storage stability samples

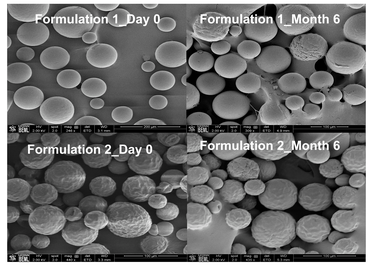

Figure 2. Comparison of morphology of real-time storage stability samples

Accelerated storage stability testing results (*i.e.* 40°C/ambient humidity and 40°C/75 %RH/8 Days):

% Drug loading remained unchanged while glass transition temperature changed slightly

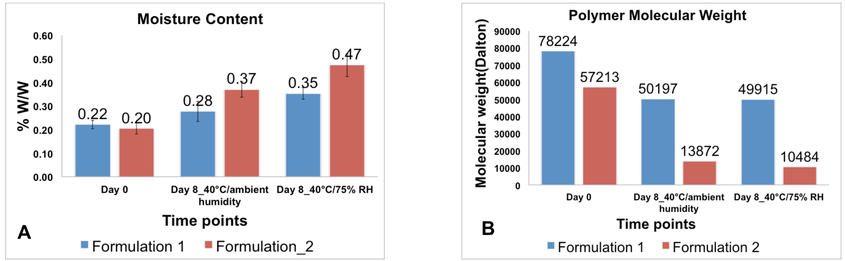

Figure 3. Effect of storage conditions on moisture content (A) and polymer molecular weight (B) of accelerated storage stability samples

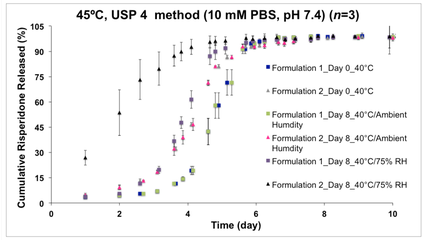

Figure 4. Comparison of *in vitro* release profiles of accelerated storage stability samples

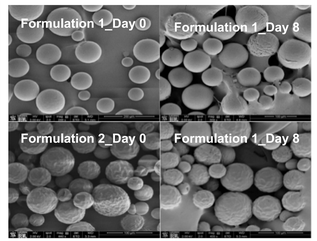

Figure 5. Comparison of morphology of accelerated storage stability samples (40°C/75 %RH)

CONCLUSIONS

1. The prepared risperidone microspheres were stable at 4°C over the 6 month test period. Physicochemical properties (such as moisture content) appeared to be critical during long-term storage of PLGA microspheres.
2. The developed accelerated USP apparatus 4 method was capable of detecting significant changes in critical physicochemical parameters of the risperidone microspheres.
3. High temperature and high moisture conditions resulted in significant microsphere degradation, suggesting that cold chain technology should be implemented to store and transfer the prepared risperidone microspheres.

REFERENCES

1. A. Rawat, D.J. Burgess, *et.al.* Validation of USP apparatus 4 method for microsphere in vitro release testing using Risperdal® Consta®. Int J Pharm,2011;420 (2):198-205.

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DISCLAIMER

- This poster reflects the views of the authors and should not be construed to represent FDA'S views or policies.