Formulation of Monodisperse Controlled-Release Quetiapine Microspheres

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ABSTRACT

Objectives

1. Demonstrate microsphere fabrication capabilities using Optimμm® technology.
2. Understand the variables to manipulate dissolution profiles of controlled-release microsphere formulations.
3. Describe how Optimμm technology delivers better particle precision compared to traditional methods.

Methods

Uniform microspheres were fabricated from a proprietary process previously described.[1] Briefly, quetiapine was dissolved in melted stearic acid and combined with other excipients (triglycerides, waxes, celluloses, etc). The mixtures were processed through a proprietary nozzle in a single step to produce matrix microspheres in the size range of ~250 μm. Various formulations were dissolution tested in vitro to evaluate controlled release performance.

Results

Uniform quetiapine microspheres were obtained with encapsulation efficiencies of up to 90%. Varying excipient content in formulations conferred the ability to tune *in vitro* release profiles of the drug. Increasing loading percentage of API increased the release kinetics of the drug, particularly at earlier time points. Moreover, increasing the average particle size decreased release rate due to decreasing the surface-to-volume ratio of the particles. Optimμm technology offers fast and efficient screening method for adjusting controlled release performance as well as downstream scalability.

[1]Berkland C., Kim K., and Pack D., "Fabrication of PLG microspheres with precisely controlled and monodisperse size distributions," Journal of Controlled Release, May 2001, 73(1):59-74.

INTRODUCTION

Quetiapine is an antipsychotic drug used for the treatment of schizophrenia, bipolar disorder and depression and is currently marketed as a QD tablet. An alternate presentation of the drug in the form of controlled release microspheres would provide flexibility of finer dose titrations and address patients with dysphagia when delivered as a suspension.

Adare's Optimμm® technology offers a unique and efficient method of fabricating monodisperse microparticles at reduced development time. The study herein uses Adare technology to fabricate monodisperse quetiapine microparticles to investigate the effects of formulation and size on the release profile of the API.

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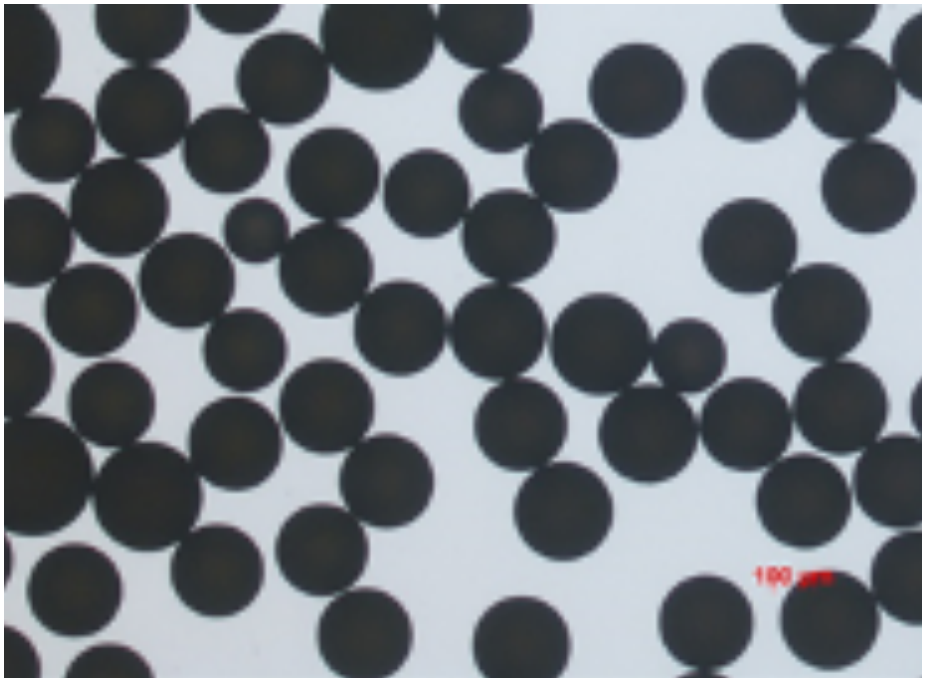

Figure 1. Representative optical microscopy image of quetiapine microspheres with D[4,3] = 254 μm.

Presenter
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Dr. Nonoyama has over 12 years of pharmaceutical formulation development experience with eight years working with particle-based delivery systems and he is currently a Principal Scientist at Adare Pharma Solutions.

Nonoyama earned his degree in Chemistry at University of South Florida, with post-doctoral training at University of Kansas, Department of Pharmaceutical Chemistry.

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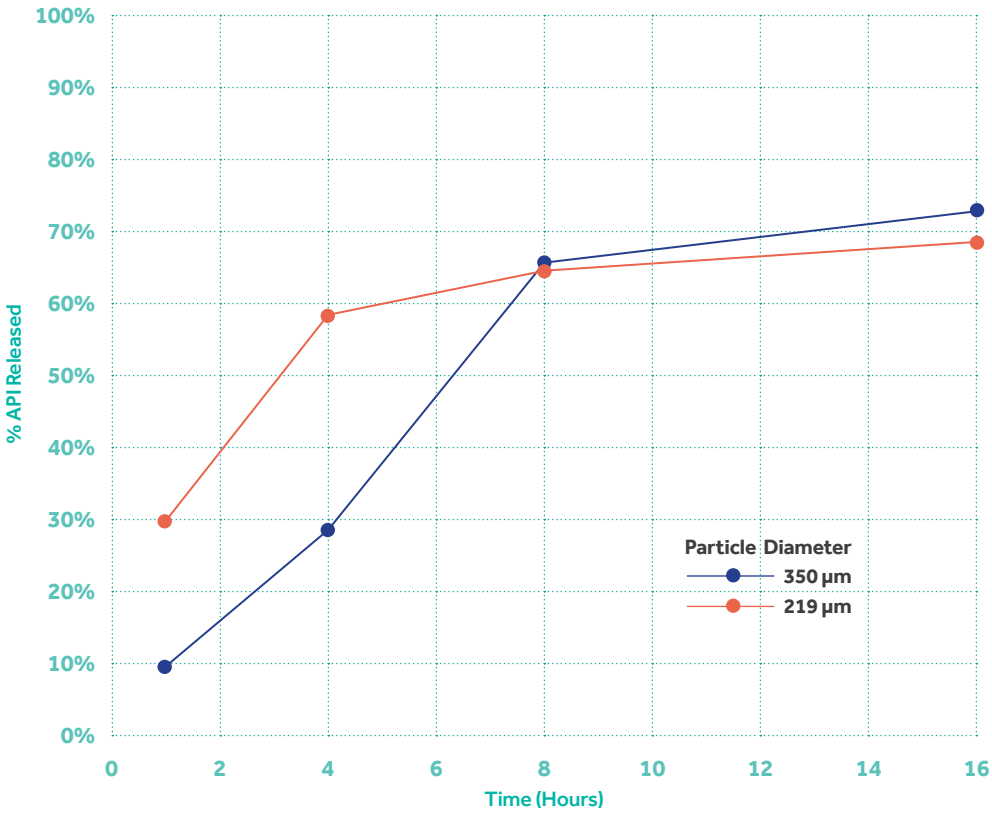

Figure 2. *In vitro* release curves of quetiapine microspheres as a function of size reflects differences in dissolution rates. Smaller particles with larger surface-to-volume ratio shows faster release rates at the earlier time points.

CONCLUSION

This study showed the ease with which Optimμm can be used as a tool to efficiently screen controlled release formulations. Various parameters of quetiapine microspheres were manipulated to demonstrate their effects on in vitro drug release. The results hold the potential for development of a powder dosage form that rivals current marketed tablets as well as a formulation that confers longer extended release.

Adare Pharma Solutions is a global technology driven CDMO providing turnkey product development through commercial manufacturing expertise focused on oral dosage forms for the Pharmaceutical, Animal Health and OTC markets. Adare's specialized technology platforms provide taste masking, ODTs, and customized drug release solutions. With a proven history in drug delivery, Adare has developed and manufactured more than 40 products sold by customers in more than 100 countries globally.