A Study of the Utilization of Starch Micro-Spheres as a Core Material for a Dry Powder Layering of an API to Facilitate High API Loading in Particles Below 250 microns

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INTRODUCTION

API layering onto multi-particulate core materials has become an increasingly popular method of drug delivery in the pharmaceutical industry in recent years. The ability to control dosing, customize the dosing rate and reduce the risk of dose dumping along with the ability to create orally disintegrating tablets (ODT's) with controlled release particles are all advantages to multi-particulate dosage forms.

One of the main challenges to this technology is controlling the size of the particles while still delivering a high payload of API on each particle. For ODT applications, size of the drug loaded particles is an important consideration as large particles lead to a gritty mouth feel. Taste masking is also normally essential in ODT applications, which requires that the particles be uniform in size and shape, as well as being smooth at the surface to facilitate repeatable taste mask performance in production. Standard core materials such as sugar starch spheres and micro-crystalline cellulose spheres are not available in sizes below 100 microns and in the size ranges of 100-300 microns, these core materials tend to be non-uniform and have low sphericity and aspect ratios which are not ideal for drug layering processes.

Processes such as extrusion/spheronization are often not able to produce high API loaded particles below 300 microns in size and require several excipients to be successful. Direct granulation/spheronization often needs to be sized after the process and typically has low efficiencies.

This study investigated whether a starch microsphere in the 50-80 micron range could be used as a core material to effectively layer a high payload of API onto while maintaining a finished particle size below 250 microns.

EQUIPMENT

Freund-Vector Corporation
Granurex® GXR-35

EXPERIMENTAL METHODS

In the dry powder layering process, 1 kg of starch microspheres (Grain Processing Corporation, Muscatine, IA USA) were loaded into a novel conical rotor processor (Granurex® GXR-35, Freund-Vector Corporation, Marion, IA USA). Four KG of micronized ibuprofen powder was loaded into a K-Tron KT-20 powder feeder and was dry layered onto the starch microspheres, using a 5% solution of PVP K-30 in water as a binder. This resulted in an 80% loading of API onto each starch particle.

The size, aspect ratio (roundness on a scale of 0.0-1.0 with 1.0 equal to a perfect circle) and sphericity (smoothness on a scale of 0.0-1.0 with 1.0 equal to a perfectly smooth surface) of the particles were monitored throughout the process utilizing a QICPIC particle size analyzer. (Sympatec) Dissolution and content uniformity of the finished coated particles was completed to confirm uniform and complete application of the API to the core material. Process efficiencies and yields were also calculated.

RESULTS AND DISCUSSION

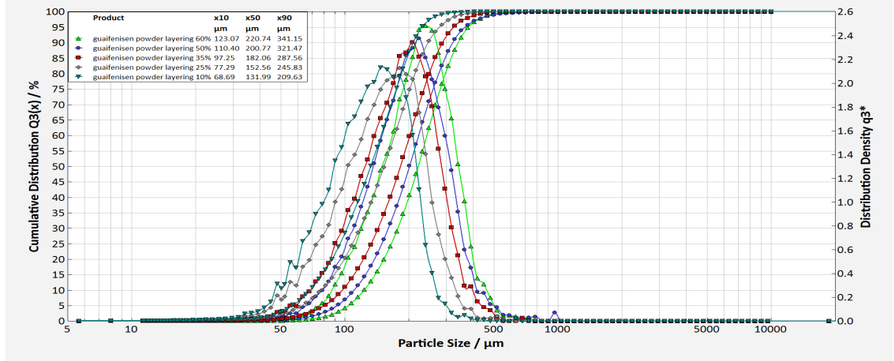

Figure 1: PSD chart showing uniform particle growth across the distribution

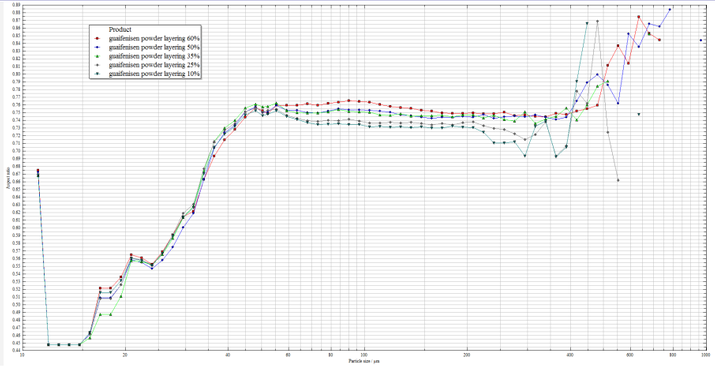

Figure 2: Aspect Ratio Chart

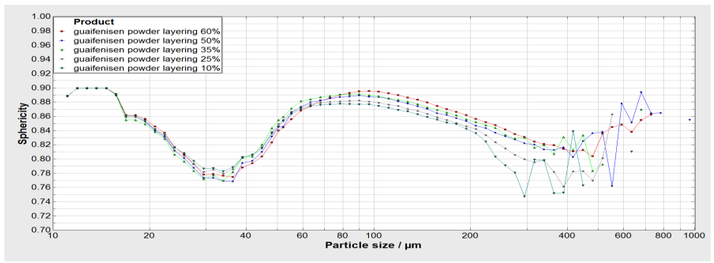

Figure 3: Sphericity Chart

Particle size analysis (PSD) throughout the drug layering process revealed steady, uniform growth across the entire population throughout the entire process. Consistent growth in the D10, D50 and D90 measurements were seen in each sample throughout the process.

Shape analysis showed a steady increase in aspect ratio (roundness) and in sphericity (smoothness) throughout the process, with the highest value being present in the finished materials.

The processes ended with yields in the 95.3-97.2% range and had agglomeration rates below 0.2%. Each batch ended with an average finished particle size of 220 microns, significantly less than the target of below 250 microns. Content uniformity and dissolution values indicated that the API was coated uniformly across all of the starch spheres with minimal loss in the coating process.

CONCLUSIONS

Using starch microspheres as a core material for drug loading of API is a viable solution for obtaining high API payloads in a finished particle size below 250 microns. The high yields, excellent size and shape characteristics and excellent content uniformity results show advantages over other methods for obtaining high API loaded particles in that size range.