A Comparison of Spherical Core Materials Used for Controlled Release Drug Layering Processes

Shawn Engels [1], Brian Jensen [1], Susan Freers [2], Ben Porter[2], Carrie Shipley[2]
[1] Freund-Vector Corporation, Marion, IA USA
[2]Grain Processing Corporation, Muscatine, IA, USA

INTRODUCTION

Three different spherical core materials for use in API layering processes; sugar/starch spheres, microcrystalline cellulose (MCC) spheres and novel maltodextrin/starch (M/S) spheres were coated with 40% Acetaminophen in a dry powder layering process. The three core materials were evaluated both before and after the drug layering for sphericity, aspect ratio, particle size distribution and friability. The novel maltodextrin/starch spheres either equaled or out-performed the more established sugar/starch and MCC spheres in each category.

METHODS

The process of dry powder drug layering was chosen to compare the different core materials. For each of the core materials, 50 KG of 20/25 mesh core material was loaded into a Granurex® GXR-95 (Freund-Vector Corporation) conical rotary fluid bed insert. 20 KG of micronized Acetaminophen powder was loaded into a KT-35 Loss-in-weight powder feeder (K-Tron), equipped with Acti-Flow® vibratory agitation. An aqueous solution of 5% PVP K-30 (BASF) was prepared for use as a binder. The Acetaminophen was applied to the core material at a rate of 200 g/minute, and the binder solution sprayed simultaneously at 100 g/min. Following the drug layering, a 25% coating of Eudragit® L30D 55 (Evonik) was applied to the drug layered beads to provide enteric protection. Processing parameters and observations were recorded and process yield and agglomeration rate were measured for each core material. Agglomeration rate was measured using a vibratory screener (Midwestern Industries) equipped with a 16 mesh and 20 mesh screen. A QICPIC (Sympatec) particle image analyzer was used to measure physical characteristics including sphericity (smoothness), aspect ratio (roundness) and particle size distribution both before and after the coating was applied.

EQUIPMENT

Freund-Vector Corporation Granurex® GXR-95

Sympatec QICPIC®

RESULTS

DISCUSSION

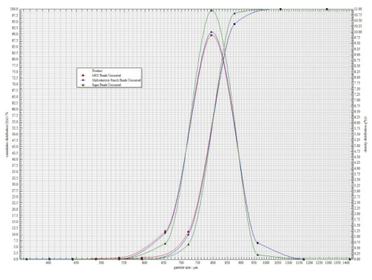
The process data and observations showed specific differences between the three types of core materials. Early in the process using the sugar beads, the beads continually showed signs of overwetting and agglomeration, including sticking to the walls of the machine and the rotor disc. As a drug coat developed on the surface of the sugar beads, the tendency towards agglomeration was diminished, and a smooth, uniform coating was applied. The drug layered beads took 25 minutes to dry below 2.5% moisture. The process using the sugar beads resulted in a 96% drug application efficiency and 5.2% agglomeration rate (over 16 mesh).

The MCC core material resulted in a much different process, as the Acetaminophen did not adhere efficiently to the surface of the cores throughout the first 20 minutes of the process. This resulted in a very dusty environment inside the rotor and a relatively lower processing efficiency. As moisture built up throughout the process, the Acetaminophen did begin to layer onto the MCC cores more efficiently. The MCC cores were insoluble in the aqueous binder being applied, so the surface of the bead did not become sticky until a significant amount of binder solution had been applied. The MCC beads did not tend to agglomerate like the sugar cores, but took significantly longer to dry than the sugar beads at 47 minutes. The drug layering efficiency was 93.1% and the agglomeration rate was 0.6%.

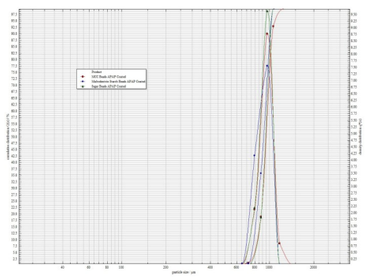
The maltodextrin/starch (M/S) beads showed no signs of agglomeration throughout the process, and also ran relatively cleaner than the other two core materials. The M/S beads did require a larger amount of binder to be applied prior to becoming sticky than the sugar beads, but less than the MCC beads, as the process remained dusty only for the first 5 minutes. The drying time was similar to the sugar beads at 26 minutes. The process resulted in a drug layering efficiency of 97.1% and an agglomeration rate of 0.8%.

The QICPIC image data showed very similar PSD profiles for both the raw and coated beads for each of the core materials with the raw sugar beads ranging from 726-860 microns, the raw MCC beads ranging from 709-867 microns and the M/S beads ranging from 715-867 microns. All had a D50 of 793 microns. The coated MCC beads had a range of 798-1055 microns, the coated sugar beads had a range of 802-1038 microns and the coated M/S beads had a range of 761-1034 microns. All of the coated beads had D50 values between 925 and 950 microns. The sphericity (smoothness on a scale of 0.0-1.0, with 1.0 being perfectly smooth) [2] measurement indicated that again all three core materials were very similar, with the sugar and MCC beads having a slightly smoother surface than the S/M raw beads at 0.895, 0.891 and 0.875 respectively. The coated beads showed no difference in sphericity between the three. The aspect ratio (roundness measured from 0.0-1.0 with 1.0 being a perfect circle) [2] measurement also showed very similar values for each of the three materials, although the MCC beads were significantly less round at the lower end of the PSD with a value of only 0.745, while the sugar and M/S beads had values of 0.840 and 0.851 at the same particle size. The MCC improved dramatically in the middle and upper ends of the PSD to a value of 0.842. The aspect ratio remained relatively the same in the coated materials.

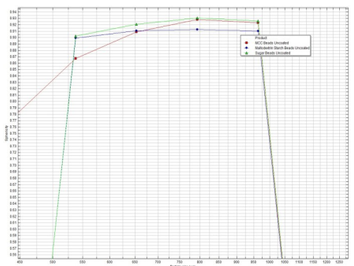
PARTICLE SIZE AND SHAPE CHARTS



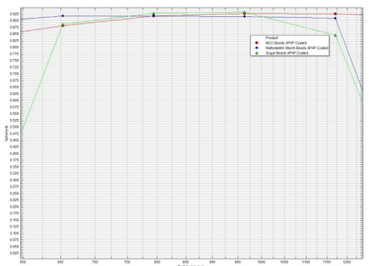
Raw Beads (PSD)



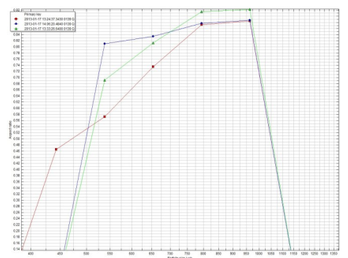
Coated Beads (PSD)



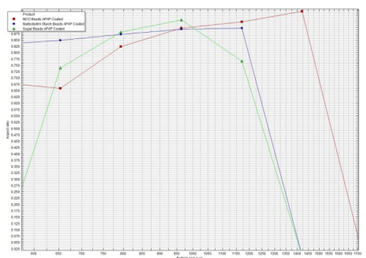
Raw Beads (Sphericity)



Coated Beads (Sphericity)



Raw Beads (Aspect Ratio)



Coated Beads (Aspect Ratio)

CONCLUSIONS

Although all three core materials in this study had very similar physical characteristics and produced similar results in the finished beads, there were significant differences in the way each behaved in the drug layering process. The sugar beads moisture sensitivity early in the process caused problems with controlling the agglomeration and sticking present. While those issues largely went away once a sufficient drug layer was on the beads, it could cause problems with aqueous coating systems. The MCC beads did not have the same moisture sensitivity issues as the sugar, but did require significantly more binder to be applied before being able to adhere the drug efficiently. The MCC beads also tended to hold on to moisture throughout the process, which could be an issue for moisture sensitive drugs. The M/S beads performed well in the areas that the other two materials showed weaknesses, and also compared favorably to the other beads in all of the physical tests. The M/S cores could be a viable solution for processes that have difficulties due to agglomeration or moisture sensitivity of the API where sugar and MCC cores may cause issues.