A Comparison of Content Uniformity and Dissolution of API Applied to Different Spherical Core Materials Using a Controlled Release Drug Layering Process

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PURPOSE

To investigate the process of dry powder drug layering and enteric coating on three spherical core materials: two traditional cores, sugar/starch and microcrystalline cellulose, and a newer type of core manufactured from starch and maltodextrin. To compare dissolution and content uniformity for the Active Pharmaceutical Ingredient (API) applied at different percentages on powder layered cores and enteric coated finished spheres.

METHODS

This study included three spherical cores manufactured from 1.) sugar/starch (sugar spheres), 2.) microcrystalline cellulose (MCC spheres) and 3.) starch/maltodextrin (starch spheres). API (acetaminophen [APAP]) was dry powder layered onto the cores at 1%, 2%, 5%, 20% and 40% (by weight basis) using a Granurex GXR-95 conical rotary fluid bed insert (Freund-Vector Corporation). The API was applied to 50 kg of 20/25 mesh cores using a KT-35 loss-in-weight powder feeder (K-Tron) equipped with ActiFlow vibratory agitation. An aqueous binding solution of 5% PVP (BASF K-30) was applied at 100 g/minute with the API applied at 200 g/minute. The 40% powder layered cores were enteric coated with a 25% coating of Eudragit L30D (Evonik). Dissolution was tested by UV absorbance on all uncoated and enteric coated cores using a Distek Evolution 6100 USP35 Apparatus 1 at 100 rpm and 37°C (n=6) per USP procedure. A 1.0 g sample was tested for spheres layered with 1% and 2% API, a 0.5 g sample for 5% API and a 0.15 g sample for 20% and 40% API. Content uniformity was determined for each core type by UV absorbance (n=3).

RESULTS

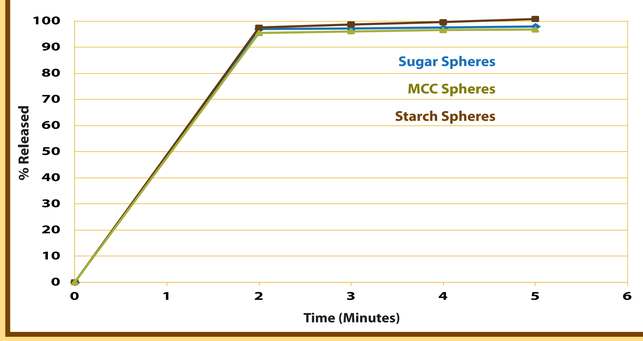
All three core types processed well; however, the sugar/starch spheres showed a higher degree of agglomeration than the other two spheres and the agglomeration occurred earlier in the process than with the other spheres. The microcrystalline cellulose cores took longer to dry than the other two types of spheres. The starch/maltodextrin spheres ran the cleanest in the equipment. All three cores resulted in acceptable finished product. All uncoated core samples released 100% of the API within 2 minutes. The API release rate of all enteric coated spheres in 0.1 N HCl was less than 2.5% within 2 hours and was greater than 90% within 10 minutes in 6.8 pH phosphate buffer solution (PBS). Content uniformity results were good for all samples tested.

CONCLUSIONS

Viable controlled release spheres can be successfully manufactured using a powder layering process on a variety of core substrates. Dissolution and content uniformity results were equivalent for all the finished cores; however, the starch/maltodextrin cores were easier to process.

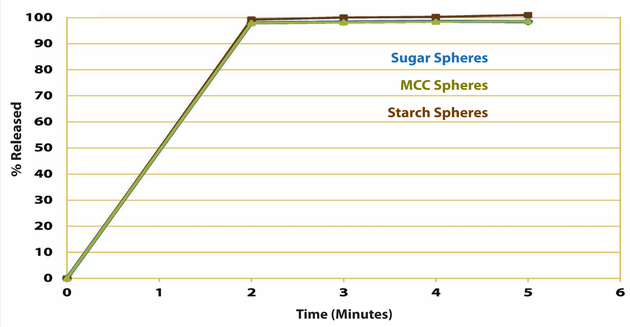
RELEASE FROM UNCOATED SPHERES LAYERED WITH 1% APAP

0.1 N HCl



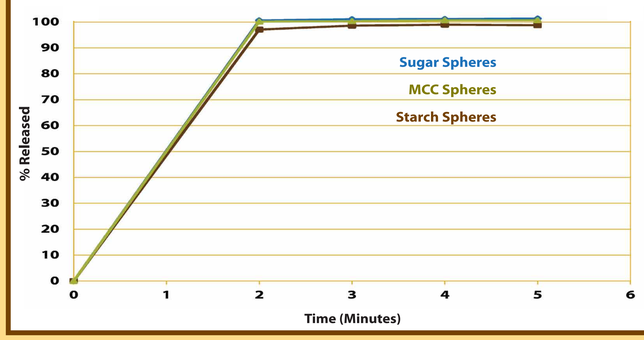
RELEASE FROM UNCOATED SPHERES LAYERED WITH 2% APAP

0.1 N HCl



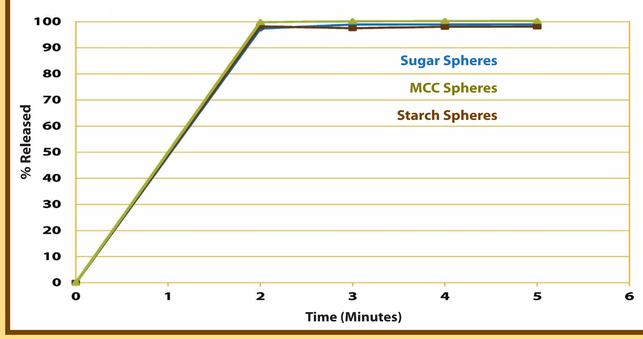
RELEASE FROM UNCOATED SPHERES LAYERED WITH 5% APAP

0.1 N HCl



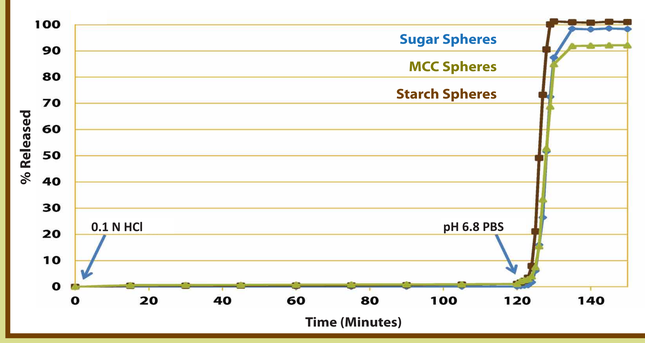
RELEASE FROM UNCOATED SPHERES LAYERED WITH 20% APAP

0.1 N HCl



RELEASE FROM ENTERIC COATED SPHERES LAYERED WITH 40% APAP

0.1 N HCl (FIRST 2 HRS.) & pH 6.8 PBS (AFTER 2 HRS.)



RELEASE FROM ENTERIC COATED STARCH SPHERES LAYERED WITH 40% APAP

0.1 N HCl (FIRST 2 HRS.) & pH 6.8 PBS (AFTER 2 HRS.)