Effect of Coating Systems on the Dissolution and Mechanical Properties of Drug-Loaded Pellets

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Objectives

To evaluate dissolution and mechanical properties of extended-release (ER) coated drug loaded pellets, the drug loaded pellets were coated with different ER polymers using both aqueous and solvent coating systems. Sub-coating layer, top-coating layer and various polymers and their combinations were also evaluated.

Background

Extrusion/spheronization process has been widely utilized to prepare pellets with high drug loading for better size/shape uniformity and high density as compared with other alternative technologies for pellet preparation. This process provides pellets for further controlled release coating with consistent surface area and release profile due to better size and shape uniformity[1].

When the coated pellets are compressed to form tablets, the mechanical properties of the uncoated core and coating formulation will have significant effect on the integrity of the coated pellets during the compaction of the coated pellets[2-3].

Pellets loaded with a water soluble model drug were coated with ethylcellulose solutions or aqueous dispersions. Different kinds and levels of polymers were added into the ethylcellulose solvent solutions or aqueous dispersions. Methocel® E5 Premium was used as subcoat and/or topcoat. Mechanical properties of various sizes of drug loaded and coated pellets were characterized by a Texture Analyzer XT Plus. The drug dissolution was determined using USP apparatus I.

Materials

P158, a water soluble drug, is granulated with microcrystalline cellulose (MCC) PH 101 in a high shear granulator with varying amount of water with or without hydroxypropylmethylcellulose (HPMC, Methocel E5, Dow Chemical) as binder. The pellets were prepared by extrusion spheronization process and then dried in a fluid bed. The pellets were coated with aqueous or organic solution of ethylcellulose coating system. The coating was applied to the pellets by a Hüttlin Mycrolab multifunctional fluid bed processor equipped with a bottom sprayer.

Methods

The mechanical properties of the uncoated and coated pellets were characterized by Texture Analyzer XT Plus under compression mode. The texture analyzer was equipped with a 5 kg load cell (Texture Technologies Corp., Scarsdale, NY/Stable Micro System, Godalming, UK) using a 4mm round flat end steel probe.

The coated pellets (40%) with 25% MCC, 15% corn starch, glyceryl behenate (17%) and croscarmellose sodium (3.0%) were compressed into tablets. The dissolution of coated pellets and tablets were conducted in 500 ml phosphate buffer at pH 6.8 using USP apparatus 1 at 50 rpm with online UVmethod.

Results and Discussion

The force – strain curve for the compression of pellets using the Texture Analyzer is shown in Fig. 1. The first breaking force of the pellets is affected by the size of the pellets and coating. The first breaking force of the pellets was used to characterize the mechanical strength of the pellets of similar size. The coated pellet has higher breaking force as compared with the uncoated pellets. The coating can significantly increase the mechanical strength of pellets.

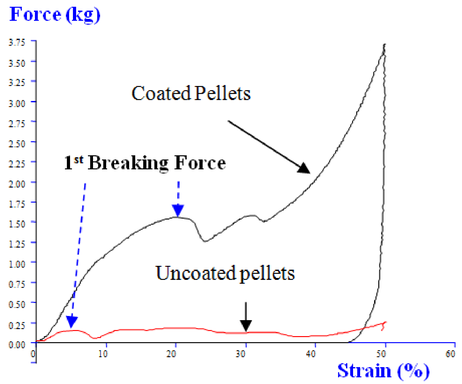

Figure 1. Force – strain curve for the pellets under compression.

The water content used in the granulation can significantly increase the first breaking force of the uncoated pellets. The binder content in the granulation formulation also affects the first breaking force of the uncoated pellets.

Higher water and binder content can increase the mechanical integrity of the pellets. However, if the water and binder content is too high, it is difficult to break the extrudates into smaller segments for spheronization, and the spheronized particles can be agglomerated due to the tackiness of the material. The formulation containing 27.5% water and 3.0% binder were selected for pellet extrusion and spheronization. The resulting pellets have a first breaking force of approximately 540 g.

The mechanical integrity of the coated pellets can be improved by the application of coating on the pellets. The mechanical integrity can increase with increasing coating thickness in term of coating weight gain. The first breaking force increases with coating level, as shown in Figure 2.

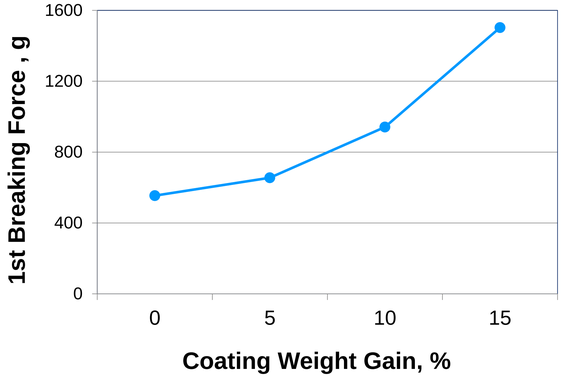

Figure 2. The effect of coating weight gain on the first breaking force of coated pellets.

The dissolution results of the coated pellets and compressed tablet at 6 kN is shown in Figure 3.

As can be seen from Figure 3, there is no significant difference in drug release between coated pellets and compressed tablets. This indicated the mechanical strength of coated pellets is higher enough to withstand the compression force .

The integrity of coated pellets during tablet compaction may also be affected by the strength of pellets and the compaction force.

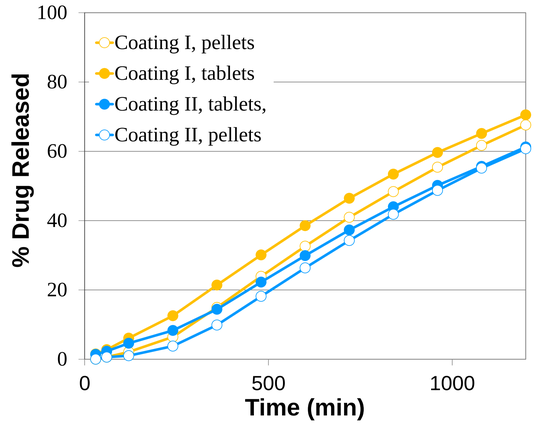

Figure 3. Dissolution of P158 from coated pellets and compressed tablets.

Conclusions

Compared to aqueous coating systems, the solvent coating formulations can form dense and low permeable film, slow drug release and increase mechanical strength of ER pellets. The polymers added in the ethylcellulose solutions or aqueous dispersions may modify the drug release profiles and change mechanical strength of coated pellets. High mechanical strength can prevent the ER coated pellets from breaking during packaging and other applications.

References

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