

Thesis Title Release of Diltiazem Hydrochloride from
Film-Coated Pellets Compressed into Tablets
and Mechanical Properties of the Film

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ABSTRACT

The mechanical properties of ethylcellulose films, such as breaking strength and tensile properties were determined in order to evaluate the effects of polymer type, plasticizer type and concentration, and dispersed solid. The tensile test of free films was found to give more reliable results. The concentration of propylene glycol was shown to exhibit no significant effect on the mean ultimate tensile strength while that of diethyl phthalate did. Both propylene glycol and diethyl phthalate were also found to have significant effect on the film elongation. Ethylcellulose film formulation plasticized with propylene glycol at 10 % w/w was therefore selected to coat the pellets.

The ratio of drug layered onto non-pareil seeds was also another factor found to play an important role on the drug release rate *via* the effectively exposed surface area

of pellets to the dissolution medium. A high percent coating level or the thicker film was required for pellets with lower drug-layered ratio in order to obtain the same drug release rate. Theoretical calculations revealed that the release of diltiazem hydrochloride from ethylcellulose film coated pellets could be described by the combination of constant and non-constant activity source diffusion-controlled model. The former model was operative as long as the solid drug still remained in the system and the release rate was zero-order. Immediately after the solid drug had completely dissolved the latter became operative and the release rate followed the non-constant membrane diffusion-controlled model.

A dramatical modification in drug release characteristics was observed after the film coated pellets had been compressed into tablet. However, the increase in compression force within the working range (400, 600, and 800 lb) was distinctly found to slightly affect the release characteristics from the compressed pellets. These modifications may not be caused by flaws or failures within the film, yet the appreciable alterations in some physical properties of the film itself under pressure instead. Finally, the electron photomicrographs of both uncompressed and compressed coated pellets were taken and assessed, which undoubtedly confirmed such hypothesis.