Interpolymer Complexation between Copovidone and Carbopol and Its Effect on Drug Release from Matrix Tablets
F. Zhang, F. Meng, Z. Wang, W. NA
University of Texas at Austin

Purpose
The objectives of the current study are: (1) to characterize the interpolymer complexation between copovidone and Carbopol 907 as a function of pH, (2) to study the material properties of the interpolymer complex, (3) to apply in situ complexation to modify the release of theophylline from Carbopol 907 matrix tablets, and (4) to investigate the effect of dissolution medium pH and in situ complexation on the characteristics and mechanisms of drug release.

Methods
We studied the effect of pH on the interactions between these two polymers using turbidity and solution viscosity methods. We utilized FT-IR to characterize the hydrogen bond interaction between these two polymers in the interpolymer complex. We fully characterized various physicochemical properties (e.g., thermal properties, hygroscopicity) of the complex. We applied solution-state $^{13}$C NMR to quantitate the weight ratio between copovidone and Carbopol 907 in the complex. Finally, we also used dissolution testing to investigate the effect of interpolymer complexation due to the presence of copovidone on the drug release of Carbopol 907–based matrix tablets.

Results
The interaction between copovidone and Carbopol 907 is pH dependent. When the pH of an aqueous solution fell below pH 4.5, a water-insoluble complex began to form and precipitate. This complex resulted from a hydrogen bond-induced interaction between the carboxylic groups in Carbopol 907 and the carbonyl groups of N-vinylpyrrolidone repeat units in copovidone. Consisting of these two polymers at an approximate 1:1 weight ratio, the complex was an amorphous material with a glass transition temperature of 157 $^\circ$C. The interpolymer complexation in situ was applied to modify the drug release properties of Carbopol 907–based theophylline matrix tablets. The effect of copovidone on drug release was dependent on the pH of the dissolution medium. In a 0.1 N hydrochloride acid solution at pH 1.2 and a 50 mM acetate buffer at pH 4.0, an insoluble tablet matrix was formed as a result of the in situ interpolymer complexation, and theophylline was therefore released via Fickian diffusion. In a 50 mM phosphate buffer at pH 6.8, drug release from the matrix tablets was still impacted by the in situ interpolymer complexation because of the low-pH microenvironment induced by Carbopol 907. As a result, the drug release rate of the matrix tablet containing both polymers at pH 6.8 was slower than that of the matrix tablets containing individual polymers. We observed similar drug release rates at both pH 1.2 and pH 6.8 between tablets containing the physical blend of these two polymers and tablets containing preformed interpolymer complexes.

Conclusion
The current study clearly demonstrated the pH-dependent interpolymer complexation between copovidone and Carbopol 907. The release of theophylline from tablets containing both polymers was dependent on the in-situ interaction between these two polymers.