Developing Analytical Methods for In Vitro Comparative Nasogastric (NG) Tube Studies of Esomeprazole Magnesium Delayed Release Capsules
A. S. Hoover, D. Sun, H. Wen, W. Jiang, M. Cui, D. Keire, C. Guo
U.S. Food and Drug Administration

Purpose
Many acid labile drugs are formulated with enteric coatings to prevent degradation within the stomach. However, the enteric coating can be damaged when drugs are suspended in water and delivered through NG tubes. The objective of this work is to develop in vitro methods to monitor the integrity of the enteric coating after water pretreatment and delivery through a NG tube.

Methods
Analytical methods for testing acid resistance stability, pH change and particle size distribution (PSD) of Nexium granules delivered through NG tubes were developed. These methods were used for testing two dosage strengths (20 mg and 40 mg), two water pretreatment times (0 min and 15 min), and three water sources with pHs ranging from 6 to 9. The contents of a capsule were transferred to an oral syringe and delivered through an 8 French NG tube prior to acid resistance, pH, and PSD analysis. Acid resistance stability, (i.e., the amount of drug released after 2-hour acid dissolution) was determined by HPLC. Particle size distributions were measured with a Malvern Mastersizer 3000 Laser diffraction system.

Results
After pretreatment with water at pHs from 6 to 9 and immediate delivery through an NG tube, the enteric coating of the Nexium granules was not damaged and less than 10% of the drug was released during the acid resistance test. By contrast, the enteric coating of the higher dosage strength was damaged after a 15 minute water pretreatment, leading to significant drug release (up to 51 ± 8%) during the acid resistance test. Of note, the enteric coating of the granules in the lower dosage strength was not damaged during the 15 min water pretreatment. A similar trend was also observed in PSD analysis. In the case of 40 mg Nexium granules delivered through NG tubes after 15 min water pretreatment, a group of smaller particles, in addition to the large granules, was observed. The smaller particles may be debris from the damaged coating.

Conclusion
Analytical methods were developed to study the effect of incubation time and different types of water with various pHs on the integrity of enteric coatings of Nexium capsules delivered through NG tubes. The 20 mg and 40 mg Nexium capsules, delivered through NG tubes after 15 min incubation, showed different acid resistance stability and PSD results. The reason for this difference is under investigation. The methods developed in this study could be used to evaluate in vitro equivalence, and to distinguish batches with suboptimal product quality for oral drug products that can be delivered using NG tubes.

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