Use of Physiological Bicarbonate Buffers Provides More Realistic Behavior of Sustained Release Formulations Compared to Compendial Phosphate Buffers
H. A. Merchant, A. W. Basit
University College London

Purpose
To achieve a zero-order sustained release profile from an oral formulation is challenging. This study has employed a novel dynamic dissolution system which simulates the entire gastrointestinal pH from gastric to colonic compartments using bicarbonate buffer to evaluate a sustained release formulation of ibuprofen.

Methods
Ibuprofen release from Nurofen SR 300 mg (sustained release beads in a capsule shell) was tested using USP-II apparatus in 0.1 M HCl for 2 hours and subsequently in phosphate or physiological bicarbonate buffer under dynamic dissolution conditions. In the dynamic setting, the tablets were exposed to pH conditions simulating the entire gastrointestinal tract without any media change. The pH was modulated and maintained using an Auto pH(TM) system mimicking the aboral change in gastrointestinal pH.

Results
Nurofen capsules showed a zero-order sustained release profile in bicarbonate buffers under dynamic conditions simulating the entire gastrointestinal pH spectrum, whereas drug release was very rapid when tested in compendial phosphate buffers. More than 85% drug was released in two hours post-gastric phase when tested in compendial phosphate buffers, whereas it took more than 16 hours to reach the same level in dynamic conditions using bicarbonate media. The published literature indicates an increase in the elimination half-life of Nurofen SR up to 8 hours compared to only 2 hours with its immediate release counterpart. This suggests that dissolution testing in bicarbonate buffer using dynamic simulation provides more realistic insights into the behavior of sustained release formulations.

Conclusion
The Nurofen SR product displayed a zero-order sustained release profile when tested across the full range of gastrointestinal pH using an Auto-pH(TM) system, simulating the pH of gastric, proximal and distal small intestine, and the colonic environment without the need for any physical buffer change. This sustained-release behavior was in agreement with the published clinical observation. Compendial phosphate buffer, in contrast, failed to demonstrate such a sustained-release behavior and showed a pseudo-dose dumping.