consists of a drug-loaded core surrounded by two additional layers of coatings. For this study, the analgesic antipyrine was chosen as a model drug. This was selected because it is easily detectable by HPLC methods, and can be detected in the saliva of human subjects following administration. The drug-loaded core is first coated with hydroxypropylmethylcellulose (HPMC), which is responsible for a lag phase preceding the release of drug from the core. The HPMC layer is then coated with a gastroresistant film containing Eudragit L30D™ (Röhm America, Piscataway, NJ, USA), so the system is expected to remain intact as long as it remains in the stomach. The approach, therefore, relies on the relative consistency of the SITT, which is 3–5 h on average, independent of the fasted or fed condition of the subject. A pH change occurs with the passage of the system from the stomach to the duodenal environment, and the gastroresistant film then dissolves. The thickness of the now exposed HPMC coating determines the length of the lag phase before release of the drug in the core, and the thickness can be adjusted so that the lag phase corresponds to the SITT.

In vitro-release studies in a 24-paddle apparatus confirmed that the thickness of the HPMC coating had a direct correlation to the duration of the lag phase before release of antipyrine from the core. Drug-loaded cores with no coating released 100% of the antipyrine within the first hour. Cores coated with various thicknesses of HPMC exhibited a linear release of drug, with the longest release time (ca. 12 h) corresponding to the thickest HPMC coating. Tablets with the second, gastroresistant coating were demonstrated to withstand acidic pH; no drug was released in simulated gastric fluid. In simulated intestinal fluid, the gastroresistant film dissolves, and the drug-release time observed from these tablets was similar to tablets without the gastroresistant film, except for a correspondingly longer lag time associated with the dissolution time of the gastroresistant film.

The successful application of this system for delayed, colon-specific release of antipyrine was then demonstrated in a small group of healthy male volunteers (n = 4, age 36–45 years, weight 70–80 kg). The volunteers were dosed with the various formulations of coated antipyrine-loaded cores, and saliva samples were collected at 0, 0.5, 1–18, 24, 30, 36 and 48 h after dosing. Antipyrine in saliva was then quantified by HPLC. The uncoated antipyrine-loaded core exhibits essentially no lag phase. Antipyrine-loaded cores coated only with various thicknesses of HPMC coating led to a delayed appearance of antipyrine in saliva. The lag phase increases with the applied thickness of the HPMC layer, so that the thickest HPMC coating causes a lag time of ~4 h before the appearance of antipyrine. The area under the curve values for all the formulations are similar, but the corresponding peak saliva levels of antipyrine tend to decrease as the thickness of the HPMC layer increases. Antipyrine-loaded cores coated with both HPMC and the gastroresistant film exhibit similar release patterns, except for longer lag times. The enteric film prevents interaction between the HPMC coating and GI fluid until the system exits the stomach. The resulting increase in lag times was ~2 h for all formulations.

A gamma-scintigraphic study was also undertaken. Although the details will not be elaborated on here, the results of this study confirm that this drug-delivery system disintegrates and delivers drug in the caecum and/or ascending colon. These initial results show promise for the potential application of this drug-delivery system for the delayed release and/or colonic delivery of a model drug. If the application can be extended to other drugs, particularly those with low oral bioavailability or those used for the treatment of colonic disorders, it could be of significant use.

1 Sangalli, M.E. *et al.* (2001) In-vitro and in-vivo evaluation of an oral system for time and/or site-specific drug delivery. *J. Control. Release* 73, 103-110

John Weidner
Scientist, Parallel Synthesis
Medicinal Chemistry
Emisphere Technologies
765 Old Saw Mill River Road
Tarrytown
NY 10591, USA
tel: +1 914 785 4792
fax: +1 914 593 8250
e-mail: Jweidner@emisphere.com

Errata

Please note a correction to 'A genomic perspective on human proteases as drug targets' by Christopher Southan published in *Drug Discovery Today* 6(13), 681–688. On page 684, first column, line five should have read '…the reported β-secretase (BACE) mRNA…'. Also, on page 685, the first line of the legend to Figure 1 should have read '…information available for β-secretase (BACE/ASP2).'

The Editorial team of *Drug Discovery Today* would like to apologize for this inaccuracy and for any confusion that we might have caused.

1359-6446/01/$ – see front matter PII: S1359-6446(01)02004-9