### Introduction
Hydrophilic matrix systems are the most popular technology used in oral extended release (ER) drug delivery. For the purpose of achieving extended release of a high dose and highly water soluble drug, rapid hydration and strong gel layer formation of the rate controlling polymer are essential. For this purpose, generally a high viscosity grade of hydroxethyl cellulose is used in the manufacture of such matrix formulations. However, the highly soluble drug available at and adjacent to the surface of ER the tablet dissolves immediately upon contact with the dissolution media, prior to formation of the gel layer. This gives rise to an initial burst release followed by controlled release of the drug. It has been reported that barrier membrane (BM) coating of matrices may help to suppress the initial burst release. The aim of the present study was to investigate the robustness of in-vitro drug release from BM-coated hydrophilic matrix tablets of metoprolol tartrate, a BCS class I drug, in media representing typical physicochemical properties of fasted and fed state gastrointestinal fluids.

### Methods
#### Formulation and Tablet Preparation
Extended release hydrophilic matrix tablets of metoprolol tartrate (see table 1 for composition) were formulated using high viscosity hydroxethyl cellulose as a rate-limiting polymer. The BM coating consisted of aqueous ethylcellulose dispersion (Surelease E-7-19010) and an HPMC-based OpadryTM system, as pore former (85:15 w/w), was applied onto the matrices at 4% w/w weight gain to eliminate a burst release from uncoated matrices, generally observed for highly soluble drugs.

### Dissolution Studies
Uncoated and BM-coated matrices were subjected to various dissolution studies. Initially, drug release from BM-coated matrices was evaluated in USP apparatus III (RRT 10, Erweka, Heusenstamm, Germany). Figure 1 simulating the pH gradient during a fasted and fed state passage through the human gastrointestinal (GI) tract (Tables 2-3). Subsequently, experiments were performed in the Mini-Paddle apparatus (DT 600, Erweka, Heusenstamm, Germany) using 200 mL of medium and a stirring speed of 100 rpm. To simulate additional relevant physiological changes of the GI fluid composition, particularly the increase in osmolality and the decrease in surface tension after food intake, the osmolality or the surface tension of the media was varied by applying different concentrations of NaCl or sucrose or different concentrations of SLS or Tween 80, respectively, while the pH was kept constant (Blank FaSSIF pH 6.8). The magnitude of variation in osmolality and surface tension was according to the physiological relevance of human gastrointestinal tract under fed and fasted conditions. All experiments were run in triplicate. Samples were taken at predetermined time points and after appropriate dilution were analyzed at 272 nm using a UV-spectrophotometer (U 2000, Hitachi Ltd, Tokyo, Japan).

### Results
#### Impact of pH variations on drug release
Figures 1 and 2 show drug release for BM-coated hydrophilic metoprolol tartrate (MPT) matrices under pH-conditions of a simulated fasted and fed state GI passage. It is evident that pH variation within the physiological range in the GI tract did not affect drug release.

![Drug release (mean of n=3±SD) from BM-coated MPT matrices in a fasted pH gradient: 200 mL/wt/vessel, 10 rpm](image1)

#### Impact of osmolality and surface tension on drug release
Figures 3 and 4 show drug release for BM-coated and uncoated MPT matrices in Blank FaSSIF pH 6.8 adjusted to physiologically relevant osmolarities of 100 to 600 mosmol/kg and with 0.001 to 0.1% surfactant added. The release profiles presented in Figures 3 and 4 indicate that drug release from both uncoated and BM-coated matrices is controlled and independent of the osmolality and the concentration of surfactants. In addition, the impact of the BM-coating becomes visible in a reliable and highly controlled release profile which even under worst conditions (very high/low osmolality and very high concentrations of surfactants) prevents a burst release.

### Conclusion
BM-coated hydrophilic matrices represent a very promising approach for obtaining a controlled and robust release of metoprolol tartrate by eliminating the observed burst release. In future experiments it needs to be shown, if the same approach would offer similar advantages for other BCS class I drugs and, even more interesting, if it is also applicable to BCS class II compounds.

### References
2. V.O. Dias et al., Modulation of drug release from HPMC matrices. AAPS meeting, San Antonio, TX, November 2006 (pPoster)