Effect of In Vitro Biorelevant Stress Conditions on Drug Release from EUDRAGIT® NM 30D Based Matrix Tablets

A. Engel, V. Jain, A. Guha, S. Joshi
Evonik Industries

Purpose
The aim of this investigation was to evaluate effect of in-vitro biorelevant stress conditions on drug release behavior of EUDRAGIT® NM 30D matrix tablets using Bupropion hydrochloride as a prototype drug and its comparison with Hydroxypropyl Methylcellulose (HPMC) matrix based marketed formulation.

Methods

Preparation of EUDRAGIT® NM 30D matrix tablets: Bupropion hydrochloride 200mg tablets were prepared in fluid bed processor by top spray granulation of half the quantity of Bupropion along with commonly used pharmaceutical excipients. The dispersion for granulation was prepared using EUDRAGIT® NM 30D and HPMC 3 cps in water. Prepared granules were dried in fluid bed processor at 55-60°C, until the LOD of NMT 3.5% w/w was achieved. Dried granules were then sifted through 30# ASTM sieve and blended with remaining quantity of Bupropion and other excipients, in a drum hoop mixer. Tablet compression was carried out using 12.5 mm flat circular punch with an average weight of 645 mg and hardness of 80 to 90 N. Prepared tablets were cured at 50°C for 24 hours in a tray dryer.

in-vitro drug release: in-vitro drug release was carried out on EUDRAGIT® NM 30D matrix tablets and marketed HPMC matrix tablets, in dual buffer 0.1 N HCl (2 hours) followed by pH 6.8 buffer (12 hours) using USP type II dissolution apparatus at 50 RPM. Amount of drug release was determined by HPLC.

in-vitro biorelevant mechanical stress study: A biorelevant dissolution stress test device and method described in literature was used for the test. Simulated gastric fluid with pepsin (SGF) pH 1.8 for 0.5 hours @ 100 RPM followed by Hanks bicarbonate buffer of pH 6.8 for 12 hours @ 50 RPM was used as dissolution media. Biorelevant mechanical stresses were applied using sequences of agitation including movement and pressure fluctuations alternated with static phases as observed in-vivo. Amount of the drug dissolved was determined by means of UV–Vis spectroscopy.

Stability studies: Stability study of Bupropion HCl EUDRAGIT® NM 30D matrix tablets was conducted as per ICH guidelines in closed induction sealed HDPE containers at 40°C/75% RH up to 6 months.

Results
EUDRAGIT® NM 30D based matrix tablets of Bupropion hydrochloride were successfully prepared using top spray granulation technique. In the in-vitro drug release test without application of additional mechanical stress, the observed drug release from EUDRAGIT® NM 30D based matrix tablets was faster as compared to the marketed HPMC based matrix tablets. However, in case of in-vitro biorelevant mechanical stress study, the results were reversed, with significantly higher release from marketed HPMC based matrix tablets, indicating high impact of biorelevant stresses on drug release from HPMC based matrix tablets as compared to EUDRAGIT® NM 30D based matrix tablets. EUDRAGIT® NM 30D based matrix formulation of Bupropion was stable when stored up to 6 months under ICH recommended accelerated storage conditions.

Conclusion
EUDRAGIT® NM 30D based matrix tablets were found to resist the gastrointestinal mimicking mechanical stresses better than the HPMC based marketed formulation. Further investigations with reference to this finding can provide more insights into possible variations in the in-vivo performance of HPMC based matrix products. EUDRAGIT® NM 30D based matrix formulations can effectively minimize the effect of in-vivo mechanical stress conditions on changes in drug release profiles, and thus on the product performance. The extension of these studies can be useful in providing better IVIVC predictability when EUDRAGIT® NM 30D is used as a matrix former in tablets.