conferenceseries.com JOINT EVENT

Biochem Pharmacol (Los Angel) 2018, Volume 7
DOI: 10.4172/2167-0501-C1-010

10th World Congress on Pharmacology
&
6th International Conference and Exhibition on
Advances in Chromatography & HPLC Techniques
August 02-03, 2018 | Barcelona, Spain

Optimization of a HPLC method for the analysis of related substances using DoE integrated with the steepest ascent method and Monte Carlo simulation

Gautam Samanta, Trupti Tol, Harshad Tawde, Savita Gorad, Avinash Jagdale, Amol Kulkarni, Avinash Kasbale and **Anita Desai**
Cipla Limited, India

The analytical method for the determination of related substances for formulation of tablets was optimized using quality by design approach. The selectivity issue encountered during oxidative degradation was a stumbling block, with a few poorly resolved degradant peaks (each greater than 1.0%) eluting very close to the main peak and the known impurities. Selectivity (resolution) was considered as a critical quality attribute. Buffer pH, column oven temperature, gradient slope and flow rate were the critical method variables studied through design of experiments. Discovery of an unknown impurity (named as impurity D, about 1.0%) was the key finding from the DoE study. Resolution between impurity D and the main peak and the resolution between the main peak and another impurity, impurity E, were very critical and highly sensitive to change in buffer pH. Moreover, variation in the buffer pH had opposite impact on these two responses. The peaks for API and impurity E were resolved at pH 3.0 and exhibited higher sensitivity towards pH hence the pH value was fixed to 3.0. To improve the separation between impurity D and API, column oven temperature was explored using the method of steepest ascent. Experiments were performed at different temperatures along the path of rapid increase in response, and finally at 45°C, both the critical pairs were well resolved. To achieve the global optima, a response surface methodology was employed. Finally, the optimum condition chosen was pH 3.0, column oven temperature 44°C, % MP. B 45% and flow rate 1.0 mLmin-1. Establishment of design space was complimented by accomplishment of a robust zone through Monte Carlo simulation and capability analysis. An analytical control strategy was designed to ensure that the method repeatedly meets its acceptance criteria. The QbD approach facilitated systematic optimisation of the method, despite various challenges and complications.

gautam.samanta@cipla.com