Response Surface Methodological Approach toward Optimization of RP-HPLC Method to Determine Paracetamol in Tablets

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Abstract

Response surface methodology (RSM) was applied to develop a RP-HPLC method in which paracetamol was analyzed and determined on a C18 column with UV detection. To explain more, RSM was used to statistically model the impact of flow rate (mL.min^{-1}) (**A**), column temperature (°C) (**B**) and mobile phase composition (H_2O:MeOH) (**C**) on the retention time (Rt) of Paracetamol within tablets.

Introduction: The major goal of this investigation was to optimize a RP-HPLC method which is simple, linear, accurate, sensitive and selective in determination of Paracetamol in solid dosage forms.

Methods and Results: Three distinctive levels were dedicated to each evaluated factor. Box-Behnken experimental design including seventeen independent runs within a range of 25-50% MeOH ratio (mobile phase), 25-45 ºC and 0.7-1.3 mL .min^{-1} flow rate were carried out to explore the effective factors on Rt of Paracetamol using RP-HPLC method. ANOVA results revealed that quadratic model was significant (Model F-value of 225.65) and could best describe the relationship among dependent variable (Rt) and independent ones:

$$Rt = 3.30 - 1.2A - 0.38B - 0.80C + 0.30AC + 0.43BC + 0.53A^2$$

As can be understood from the model terms, the most significant term was the solvent ratio and all the factor levels were indirectly proportional to the Rt. Moreover, the interaction of column temperature and solvent ration seemed to be more important. It was also predicted that optimum assay condition included 1:2 ratio of methanol to water, column temperature of 35ºC and mobile phase flow rate of 1.3 mL.min^{-1}. Using this optimum condition, baseline separation of the drug was achieved with a good resolution and a run time of 2.1 min. The optimized method was validated in terms of linearity, accuracy, limit of detection and limit of quantification of paracetamol within a few commercially available Paracetamol tablets.

Conclusions: The optimized RP-HPLC technique provided a convenient and efficient method toward qualitative/quantitative analysis of Paracetamol in its tablets. The improved method is also rapid and sensitive enough to be used for single tablet analysis.

Key words: Paracetamol, RP-HPLC, Response Surface Methodology, Optimization

Grants: Supports of this project by Ardabil University of Medical Sciences are acknowledged.