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HPLC Method Development for Analysis of a Multi-Component Drug Product

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Introduction

Developing a high performance liquid chromatography (HPLC) method for the analysis of compounds is a task that usually requires much expertise and is also extremely time-consuming. This becomes even more complex if the sample is a mixture of multiple components. This poster reports development and validation of a stability-indicating HPLC method for a drug productwith two API,s and 21 known impurities. The initial development work was approached by employing the quality by design principles outlined in the ICH guidelines Q8 and Q9. Based on the material, process and product attributes the method has tomeasure, the performance requirement for the HPLC method and optimum chromatographic conditions were identified. The optimum conditions are examined and further fine tuned during the development stage. The method developed was validated to ICH Q2A guidelines.

Methods & Materials

Column	Atlantis T3, 150 x 4.6 mm, 3-µm	**Run time**	60 min
Column	Temp 40°C	**Mobile phase A**	0.1% TFA (pH 2.1) – Acetonitrile (95:5 v/v)
Injection volume	10-µL	**Mobile Phase B**	0.1% TFA (pH 2.1) – Acetonitrile (5:95 v/v)
Detection	UV 210 nm and 285 nm		
Flow rate	1.0 mL/min		

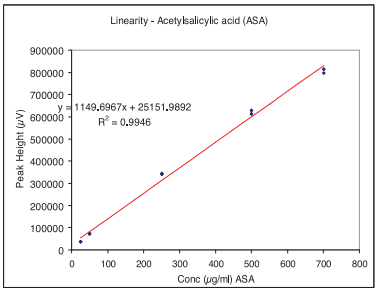
Results

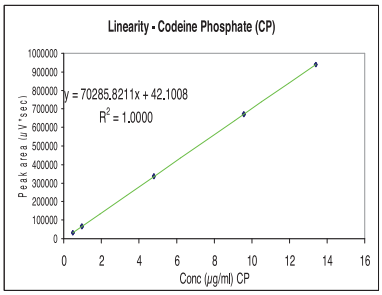
Challenges:

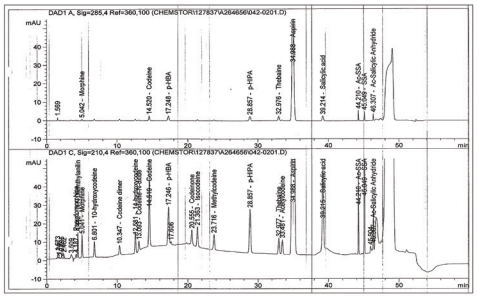
Composition: 500 mg Aspirin, 9.6 mg Codeine phosphate (CP) (@ 5 mg codeine) & 70 mg MgO
Dealing with 6 Aspirin and 15 codeine related known impurities
Low UV absorptivity of codeine/codeine related impurities
Rapid hydrolysis of Aspirin in aqueous solution
Lower solubility of Aspirin in aqueous media
Peak splitting of codeine/codeine related impurities at higher organicsolvent (>20% acetonitrile)

Requirements:

Single sample preparation for Assay and Impurities LOQ ≤ 0.04%
Resolution of critical pair ≥ 1.5
Assay and impurities to be determined using calibration curve of 30% - 130% of nominal test concentration.
Test solution should be stable at least for 6 – 8 hours (Increase of Imp. ≤0.02%)







Conclusion

A single chromatographic method was developed for both components. The method was validated for linearity, specificity, accuracy, repeatability, intermediate precision, sensitivity, robustness and range.
The method linearity was determined over the range 5% - 140% of the nominal test concentration of each API.

References
ICH guidelines Q2A, Q8 and Q9
Almac HPLC method development guidelines – AD074
Almac group guidelines on the validation and verification of analytical methods – GDE026

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