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Optimization Development and Validation of System Suitability Study for Analysis of Aceclofenac and Paracetamol in Combination Tablet Formulations by Ultra Fast Liquid Chromatography

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ABSTRACT

A simple, accurate, rapid and precise UFLC method was successfully optimised developed and validated for the quantification and detection of aceclofenac and paracetamol in combination tablet formulation. The separation was achieved by using reverse phase ODS column using a elutent consisting of acetonitrile: buffer (potassium dihydrogen phosphate) in a ratio 45:55v/v the flow rate was maintained at 1 ml/min and detection was done at 275nm using UV SPD20 detector. An ambient temperature was maintained throughout. Proposed method was optimised and validated as per ICH guidelines. The method can be employed for routine quality control analysis.

Key words: UFLC, Aceclofenac, Paracetamol.

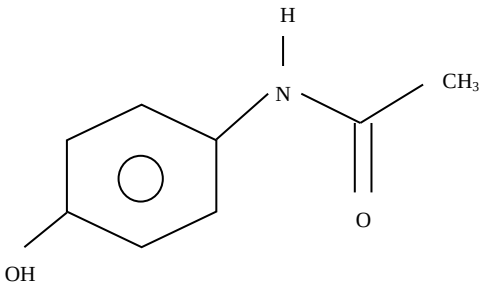
INTRODUCTION

In analytical chemistry, a highly efficient technique known as ultra-fast liquid chromatography is utilized for separating, identifying, and estimating individual components present in a mixture. This technique is based on the principle of adsorption, which involves the separation of the components according to their affinity for the stationary phase used in the process. When a mixture of compounds is introduced into the column, the components move through the stationary phase at different rates due to their varying levels of affinity for it. The stationary phase can be a solid, liquid, or gas that is capable of selectively adsorbing the individual components from the mixture. Through this process of adsorption, the individual components of the mixture can be separated and identified. This technique is highly effective as it allows for the analysis of complex mixtures with a high degree of precision and accuracy. Additionally, it is a rapid process that can be completed in a relatively short amount of time, making it a popular choice in analytical chemistry.

Ultra-fast liquid chromatography (UFLC) is a novel analytical technique that has opened up new possibilities in the field of liquid chromatography. By combining cutting-edge UFLC technology with new reversed-phase (RP) columns, it is now possible to achieve speeds that are ten times faster than those of traditional high-performance liquid chromatography (HPLC) systems. One of the major advantages of UFLC is that it offers higher resolution than traditional HPLC methods. This is because UFLC systems use smaller particle sizes in the stationary phase, which allows for better separation of components in the mixture. Additionally, the use of UFLC can result in reduced solvent consumption due to its ability to achieve high resolution with smaller elution volumes. Moreover, UFLC is a relatively new technique that is gaining popularity in the field of analytical chemistry. Its high speed and resolution make it an attractive choice for researchers and scientists who are looking for ways to streamline their analytical processes. By utilizing UFLC, researchers can save time and resources while still obtaining highly accurate and reliable results. This study focused on the optimization, development, and validation of a system suitability study for the analysis of aceclofenac and paracetamol in combination tablet formulations using ultra-fast liquid chromatography (UFLC). The goal was to establish a reliable and efficient method for analyzing these two compounds in combination, which are commonly used for pain relief and fever reduction. The UFLC method was optimized by selecting the appropriate mobile phase, column temperature, and flow rate to achieve optimal separation and resolution of the analytes. The developed method was then validated according to established guidelines for specificity, accuracy, precision, linearity, and robustness. The system suitability study was conducted to ensure that the UFLC method was suitable for its intended use by evaluating parameters such as peak symmetry, resolution, and tailing factor. The results of the system suitability study were within acceptable limits, indicating that the UFLC method is reliable and suitable for the analysis of aceclofenac and paracetamol in combination tablet formulations. In conclusion, this study successfully optimized, developed, and validated a UFLC method for the analysis of aceclofenac and paracetamol in combination tablet formulations. The system suitability study also confirmed the reliability and suitability of the developed method for routine analysis.

DRUG PROFILE

PARACETOMOL



Chemical name: N(4-hydroxy phenyl)acetamide

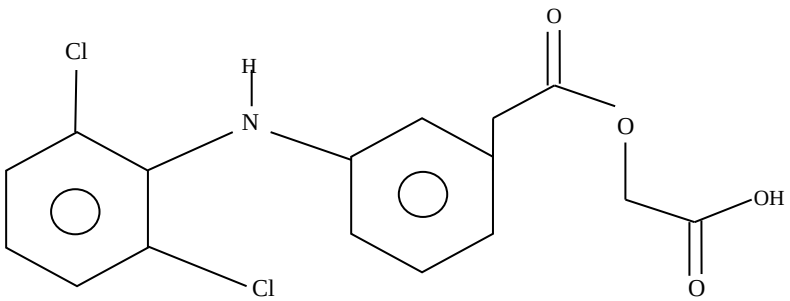
Molecular mass: 151.163g/mol

Pharmacokinetics:

- Bioavailability: 63-89%
- Protein binding: 10-25%
- Soluble in water
- Biological half life: 1-4hours

Pharmacology: Paracetamol is a widely-used medication known for its ability to relieve pain and reduce fever. It works in a similar way to non-steroidal anti-inflammatory drugs (NSAIDs) and has properties that are particularly reminiscent of cox-2 inhibitors. Paracetamol achieves its analgesic and anti-pyretic effects by inhibiting both cox-1 and cox-2, which are isoenzymes responsible for the production of prostaglandins (PGs). This inhibition is achieved through paracetamol's metabolism by the peroxidase function of these isoenzymes. As a result of this action, phenoxyl radical formation from the critical tyrosine residue, which is essential for the cyclooxygenase activity of cox-1, cox-2, and PG synthesis, is prevented. In simpler terms, paracetamol works similarly to NSAIDs and cox-2 inhibitors by inhibiting the production of prostaglandins, which are responsible for causing pain and fever in the body. This is achieved by blocking the function of two important enzymes, cox-1 and cox-2, which are involved in the production of these compounds. By inhibiting the formation of phenoxyl radicals, paracetamol is able to reduce pain and fever in individuals who use this medication.

ACECLOFENAC



Chemical name: (2-2[-[2[2,6 –dichlorophenyl)amino]phenyl] acetyl]oxyacetic acid

Molar mass: 353.0216g/mol

Pharmacokinetics:

- MP: 149-153%
- Insoluble in water

This medication belongs to the class of non-steroidal anti-inflammatory drugs (NSAIDs), which are commonly used to alleviate pain and reduce inflammation associated with conditions such as rheumatoid arthritis and osteoarthritis. The mechanism of action for this drug involves inhibiting the activity of cyclooxygenase, an enzyme that plays a critical role in the production of prostaglandins (PGs). Prostaglandins are known to contribute to pain, swelling, inflammation, and fever in the body. By inhibiting cyclooxygenase, this medication is able to decrease the production of PGs, leading to reduced

symptoms of pain and inflammation. In essence, this NSAID medication is used to alleviate pain and inflammation associated with various conditions, and its mode of action involves blocking the production of prostaglandins via inhibition of cyclooxygenase. By reducing the production of these compounds, the medication is able to provide relief from pain and inflammation.

OBJECTIVE

The goal of this project is to create and improve analytical techniques that can be used to estimate the amounts of aceclofenac and paracetamol present in various formulations, with the aim of providing economic benefits to society. The focus is on developing new, innovative methods that are cost-effective and efficient, while still producing accurate and reliable results. The end result will be the optimization of existing techniques and the development of new ones that can be used to estimate the amounts of these drugs in various formulations.

METHODOLGY

Apparatus and Software

Chromatography measurements were made on shimadzu UFLC with UV detector SPD 20 system consisting of ODS column (250*4.6mm with 5micron particle size). The system was controlled through a system controller. Data acquisition was performed with the help of software(Empower –II)Absorbance spectra were recorded using UV / VIS spectrophotometer. The rest of the calculations for the analysis were performed with Micro soft office Excel 2007 (Microsoft, USA).

Chemicals and Reagents

Working standards of paracetamol and aceclofenac were donated by Pharma analytical lab, and drugs procured from local market with brand name ACENEXT-P by CADILA pharmaceuticals. HPLC grade water, acetonitrile and potassium dihydrogen phosphate were collected from analytical lab.

Standard Preparation

Weigh accurately about 100mg of Paracetamol and 20 mg of aceclofenac working standard in a100ml volumetric flask and add 50ml of mobile phase. And shake the flask for 5minutes and sonicate for 15 minutes and make up the volume with mobile phase. Pipette out 10ml above solution in 50ml volumetric flask and make up the volume with mobile phase, shake the flask for 5 minutes.

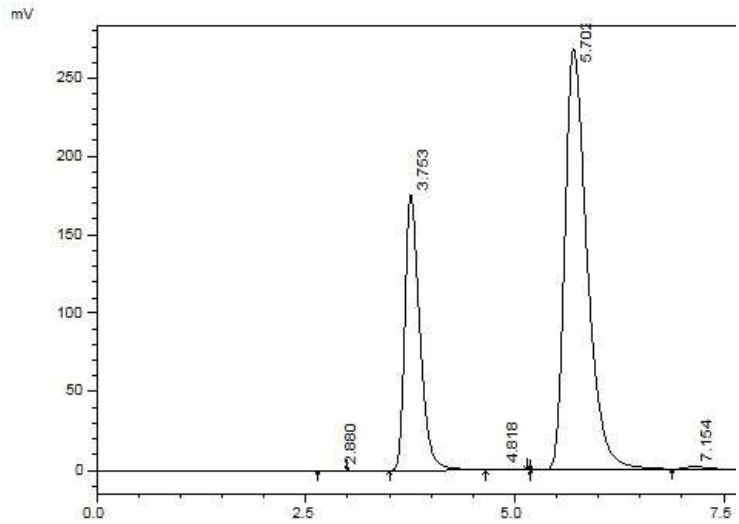
Sample Preparation

Weigh accurately 31mg of powder tablet in a 100ml volumetric flask and add 50 ml of mobile phase, and shake the flask for 5min and sonicate for 15min and make up the volume with mobile phase. Shake the flask for 5min and filter through whatman filter paper No.1 and pipette out 10ml above solution in 50ml volumetric flask and make up the volume with mobile phase. Shake the flask for 5min.

METHOD DEVELOPMENT

Several trials were performed for the method development and the best peak separation with least fronting factor was found to be the sixth trial with RT of 3.763for aceclofenac and 5.702 for paracetamol. Best peak optimal separation conditions are shown in table.

Sl. No	**Chromatographic condition**	
1	Mode of separation	Isocratic elution
2	Mobile phase	Buffer (5.5) and acetonitrile(45:55)
3	Column	ODS column (250 x4.6mm)
4	Flow rate	1.0ml/min
5	Detection wave length	275nm
6	Injection volume	20µl
7	Column temperature	Ambient
8	Run time	6min



Method Validation:

Validation studies were conducted using the final assay conditions based on the principles of validations described in ICH guidelines "Text on validation of analytical procedures" and "Q2B, validation of analytical procedures: Methodology". Key analytical parameters, including, specificity, accuracy, precision, linearity, detection limit and quantization limits were evaluated.

System Suitability:

Linearity, specificity, accuracy, limit of detection, limit of quantification, precision, robustness was studied and is shown in the table below.

Sl.No	**Parameters**	**Aceclofenac**	**Paracetamol**	**Acceptable criteria**
1	Tailing factor	1.32	1.04	Less than 2
2	Theoretical plates	3334	46820	Not less than 2000
3	Retention times	3.763	5.702	Less than 10
4	Mean area	1823789	326777	-
5	Std. Dev(Mean Area)	9401.8	1268.8	-
6	%RSD	0.5	0.4	Less than 2%

RESULTS AND DISCUSSIONS

The HPLC method was developed using a Schimadzu UFLC detector SPD20 system, which included an ODS column measuring 250x4.6mm. The mobile phase consisted of a potassium dihydrogen phosphate buffer mixed with acetonitrile in a ratio of 45:55. The flow rate was set at 1ml per minute, and UV detection was performed at a wavelength of 275nm. A 20-microliter injection volume was used with a run time of 6 minutes.To ensure the reliability and accuracy of the developed method, it was subjected to validation tests following established guidelines for specificity, linearity, accuracy, intra-day and inter-day precision, and robustness. The results of all the validation parameters were well within the acceptable criteria, indicating that the developed HPLC method is specific, accurate, precise, and robust. In summary, the HPLC method developed in this study used a Schimadzu UFLC detector SPD20 system with an ODS column and a specific mobile phase. The method was validated for various parameters, and the results demonstrated that it meets the necessary criteria for specificity, linearity, accuracy, precision, and robustness.

The system suitability parameters studied reveals that the values within the specified limit for the proposed method and are shown in the table below.

Sl.No	Parameter	Requirement	Results - Aceclofenac	Results- Paracetamol	Acceptance criteria
1	Linearity	Correlation coefficient	0.999	0.999	NLT-0.999
2	Specificity	Interference	Specific	Specific	Non- Interference
3	Accuracy and Recovery	50% 100% 150%	100.02% 100.09% 99.98	99.99% 99.76% 100.17%	
4	LOD	mcg ML^{-1}	0.57	0.51	
5	LOQ	mcg ML^{-1}	2.75	1.96	

6	Precision Intra Day Inter Day	 %RSD %RSD	 0.40 0.74	 0.59 0.63	 NMT-2%
7	Robustness	Mobile phase 43:57 47:53	0.43 0.47	0.62 0.55	NMT-2%
		Temp 28^0C 32^0C	0.51 0.41	1.39 0.5	
		Flow rate 0.9 $MLmin^{-1}$ 1.1 $MLmin^{-1}$	1.12 0.21	0.1 0.1	

CONCLUSIONS

A rapid, straightforward and economical method using ultra-fast liquid chromatography (UFLC) has been successfully developed for the simultaneous estimation of aceclofenac and paracetamol in a combination formulation. The proposed method has been thoroughly validated for various experimental parameters in accordance with ICH guidelines. The influence of the mobile phase, column temperature and flow rate has been evaluated for this method. The developed UFLC method effectively resolves and separates the aceclofenac and paracetamol analytes within a short time of only 6 minutes. Furthermore, the method exhibits excellent accuracy, precision, specificity, and robustness, making it an ideal candidate for high-throughput simultaneous determination of both drugs in combination formulations for routine analysis. a cost-effective and efficient UFLC method has been developed and validated for the simultaneous estimation of aceclofenac and paracetamol in a combination formulation. The method offers high accuracy, precision, and specificity, and can be applied to routine analysis.

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