A HPLC-BASED ANALYTICAL STUDY ON THE STABILITY OF CLAVULANIC ACID INCLUDING ORAL SUSPENSION

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ABSTRACT
The main procedural step in the pharmaceutical development phase for a new medicine or new formulation is currently stability testing. In order to guarantee that the medication is safe and effective for the duration of its shelf life, stability tests have been done to determine the appropriate storage conditions and shelf life. For drug goods, it is crucial that a material or product be stable enough to keep a given property value for a predetermined amount of time while stored under precise circumstances. For oral solution, Cefixime C16H15N5O7S2 with Clavulanate Potassium as Clavulanic Acid C8H9NO5 (50 mg/5 ml + 31.25 mg) ß-lactamase inhibitor (Clavulanic acid) and third-generation cephalosporin (Cefixime) used in combination to treat a variety of infections. Using HPLC method, the concentrations of Cefixime trihydrate and clavulanic acid brands, X, Y and Z at zero time were within the pharmacopial limit when reconstituted with distilled, decreases gradually with time and the reaction followed first order kinetics.
Keywords: Cefixime trihydrate, clavulanic acid, suspension, stability, market.

INTRODUCTION

In order to include quality, efficacy, and safety into a medicine formulation, stability testing of pharmaceutical goods is a complicated collection of processes requiring significant expense, time consumption, and scientific skill. So, stability testing assesses how the environment affects the quality of a drug ingredient or a created product, which is used to estimate how long it will last, identify the best storage conditions, and provide labeling recommendations for packaging1-4. Because the medication can be used within the stability period when it is reconstituted, it is crucial for oral suspension, thus it is crucial to fix the durability of the reconstituted sample[,6].
Cefixime and Potassium clavulanate oral suspension contain the equivalent of not less than 80 % and not more than 120 % of labelled amount of Cefixime and not less than 80 % and not more than 125 % of labelled amount of Clavulanic acid after 5 days of reconstitution when stored in Refrigerator (2 to 8 °C) and 40°C ± 2°C &75 % RH ± 5% and 25°C ± 2°C & 60 % RH ± 5%.
The chemical reactions like solvolysis, oxidation, reduction, racemization etc. that occur in the pharmaceutical products may lead to the formation of degradation product, loss of potency of activepharmaceutical ingredient (API), loss of excipient activity like antimicrobial preservative action and antioxidants etc.[7-10].

MATERIALS AND METHODS:

Chemicals: Tetrabutylammonium hydroxide (10% aqueous solution), Acetonitrile (HPLC Grade), HPLC grade water (Milli Q or equivalent), Orthophosphoric acid (AR grade).
Mobile Phase Preparation: 6.5 pH Buffer: Tetrabutylammonium hydroxide solution: Dilute 25 ml 10% Tetrabutylammonium hydroxide solution with water to obtain 1000 ml of solution and adjust the pH to 6.5 with 1.5 M phosphoric acid.
Mobile Phase:Prepare a mixture of Acetonitrile, Buffer and Water in the ratio 40: 10: 50. Filter and degas. Adjust the pH to 5.0 ± 0.1 using 1 M phosphoric acid.

Experimental Methods: The Three Brands (X, Y & Z) of Market Sample Were Reconstituted With Distilled Water and Stored At 25°c And 40°c for Seven Days Period:

Instrumentation:	
Column C-18 DB)	: 250 mm x 4.6 mm x 5 µm, ODS (preferably Supelco 516
Flow rate	: 1.5 ml/min
Detector	: UV-VIS
Wavelength	: 220 nm
Injection Volume	: 20 µl.
Column Temperature	: 30°C

RESULT AND DISCUSSION

The results of stability study show that the concentration of Cefixime trihydrate and clavulanic acid for three brand X,Y and Z collected from market at zero time were found within the pharmacopoeial limit and when reconstituted with distilled water and stored at different storage conditions decreases gradually with time.As illustrated in Table -1 the concentration of Cefixime of reconstituted oral suspension stored at 40°C decreases gradually from 108.0 % to 68.3 %, 103.5 % to 58.9 % and 109.6 % to 52.9 % of brand X,Y and Z respectively and become out of pharmacopoeial specification limit on day 3. Similarly the concentration of Cefixime at 25°C became out of pharmacopoeial specification limit on day 4 for brand X and day 7 for brand Z. Similarly the concentration of Clavulanic acid at 40°C decreases gradually from 119.3 % to 48.3 %, 115.6 % to 15.8 % and 112.8 % to 22.8 % of brand X, Y and Z respectively and become out of pharmacopoeial specification limit on day 3. Similarly the concentration of Clavulanic acid at 25°C became out of pharmacopoeial specification limit on day 4 for all the brand.

		Table 1: Assay % Result of Cefixime				
Test Interval	Brand X	Brand Y	Brand Z	Brand X	Brand Y	Brand Z
	40 °C	40 °C	40 °C	25 °C	25°C	25 °C
0 Day	108.0 %	103.5 %	109.6 %	108.0 %	103.5 %	109.6 %
Day 1	99.0 %	99.6 %	99.8 %	105.2 %	108.6 %	105.9 %
Day 2	90.3 %	86.9 %	85.3 %	99.6 %	97.8 %	101.3 %
Day 3	78.6 %	76.9 %	73.8 %	95.8 %	98.5 %	99.7 %
Day 4	76.9 %	81.9 %	76.2 %	89.3 %	96.3 %	92.8 %
Day 5	83.6 %	75.2 %	71.6 %	83.5 %	93.8 %	86.9 %
Day 6	73.5 %	71.8 %	64.3 %	70.6 %	92.9 %	88.7 %
Day 7	68.3 %	58.9 %	52.9 %	69.8 %	91.7 %	78.6 %
		Table 2: Assay % Result of Clavulanic Acid				
Test Interval	Brand X	Brand Y	Brand Z	Brand X	Brand Y	Brand Z
	40 °C	40 °C	40 °C	25 °C	25°C	25 °C

0 Day	119.3 %	115.6 %	112.8 %	119.3 %	115.6 %	112.8 %
Day 1	98.5 %	99.1 %	90.7 %	99.6 %	104.3 %	101.3 %
Day 2	90.8 %	92.3 %	89.2 %	94.6 %	97.3 %	96.5 %
Day 3	87.6 %	75.3 %	76.3 %	91.5 %	91.3 %	88.6 %
Day 4	77.6 %	65.2 %	71.3 %	89.2 %	86.1 %	70.6 %
Day 5	70.6 %	42.7 %	50.4 %	74.6 %	84.6 %	65.7 %
Day 6	63.7 %	37.3 %	41.3 %	70.8 %	52.3 %	60.4 %
Day 7	48.3 %	15.8 %	22.8 %	62.3 %	41.3 %	51.6 %

CONCLUSION

A rise in temperature increases the frequency of reactant molecule collisions, which in turn increases drug degradation. Conversely, a reduction in temperature reduces collision and decreases degradation, with outcomes that are confirmed. As a result, it is advised to keep the cefixime and clavulanic acid suspension below room temperature after reconstituting it with distilled water**.**

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