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Original Article

STABILITY EVALUATION OF AMOXICILLIIN AND POTASSIUM CLAVULANATE TABLETS USP BY ACCELERATED STUDIES

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Abstract

Stability evaluation of amoxicillin and clavulanate potassium tablets was performed as per ICH guidelines Q1A (R2).The various parameters analysed include description, assay, dissolution, water content, water activity and shelf life determination. These parameters were evaluated at zero month, 1st month, 2nd month, 3rd month and 6th month intervals. The conditions under which these parameters were analyzed include RT and accelerated conditions. The description of the tablets was evaluated as per the specifications for the time periods specified. It has been observed that there is no significant change in the description of the tablets. The assay of amoxicillin and clavulanic acid was carried out using USP HPLC method, which is designated as stability indicating method because of its capability to distinguish the degraded product with the parent one. The results of assay indicate that the tablets are within the allowable limits (90 - 120 %).The dissolution studies were carried out for the specified time intervals to study the effect of accelerated temperature and humidity on the % of drug release from the tablets. The results of the dissolution study indicate that there is no significant change in the % of drug release. The water content was determined using Karl-Fischer titrator to evaluate loss of water at higher temperatures and water uptake at higher humidity conditions. The water activity was verified using Hygrolab water activity analyzer to know the hygroscopicity of the sample at accelerated conditions. The shelf life of the tablets was found to be 48.2 months by the linear regression analysis of the stability data generated. In view of the results obtained that amoxicillin and clavulanate tablets tested are recommended to be stored at 25°C and the stability of the tablets confirmed the ICH & USFDA guidelines.

Keywords: *Stability evaluation, amoxicillin, clavulanate potassium.*

Hızlandırılmış çalışmalarda Klavulanat tabletleri ve amoksisilinin stabilite değerlendirilmesi

Amoksisilin ve potasyum klavulanat tabletlerinin stabilitelerinin değerlendirilmesi ICH'ın Q1A kılavuzuna göre yapılmıştır (R2). Tabletlerde görünüş, miktar tayini, çözünme hızı, nem içeriği ve raf ömrü gibi çeşitli parametreler incelenmiştir. Bu parametreler sıfırıncı, birinci, ikinci, üçüncü ve altıncı aylarda değerlendirilmiştir. Bu parametrelerin RT ve hızlandırılmış koşullar altında analiz edilmiştir. Tabletlerin görünüşü belirli aralıklarda spesifikasyon parametresi olarak değerlendirilmiştir. Amoksisilin ve klavulanik asit analizi, ana molekül ve parçalanma ürünlerini birbirinden ayırabildiği için stabilitenin gösterilmesi için tasarlanmış bir metod olan USP HPLC yöntemi ile yürütülmüştür. Deney sonuçları tabletlerin izin verilen sınırlar içinde olduğunu göstermektedir (90-120 %). Dissolusyon deneyleri, hızlandırılmış sıcaklık ve nemin tabletlerden % ilaç salınımına etkilerini araştırmak için belli zaman aralıklarında yapılmıştır. Sonuçlar % ilaç salınımında önemli bir değişiklik olmadığını göstermektedir. Yüksek sıcaklılardaki su kaybı ve yüksek nemdeki su çekme özellikleri Karl-Fisher'in titrasyon yöntemine göre yapılmıştır. Numunenin hızlandırılmış koşullardaki nem çekme özelliğini tespit etmek için, su aktivitesi, hygrolab su aktivitesi analizörü kullanılmıştır. Elde edilen stabilite test sonuçlarından kaynaklanan linear regresyon sonuçlarına göre tabletlerin raf ömrü 48.2 ay olarak tespit edilmiştir. Elde etmiş olduğumuz sonuçlara göre amoksisilin ve klavulanat tabletlerinin 25 °C de saklanması tavsiye edilmekte ve tabletlerin stabilitesi ICH & USFDA kılavuzlarını doğrulamaktadır.

Anahtar Kelimeler: *Stabilite değerlendirilmesi, amoksisilin, potasyum klavulanat*

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INTRODUCTION

The success of an effective formulation can be evaluated only through the stability studies. Stability testing is a routine procedure performed at various stages of product development. In early stages, accelerated stability testing, at relatively high temperatures and/or humidities can be used as a "worst case" evaluation to determine what kind of degradation products may be found after long term storage. Stability of a pharmaceutical preparation can be defined as "the capability of a particular formulation (dosage form or drug product) in a specific container – closure system to remain within its physical, chemical, microbiological, therapeutic and toxicological specification through out its shelf life."(1)

Testing under more gentle conditions, those recommended for long term shelf storage, and slightly elevated temperatures can be used to determine a products shelf life and expiration dates. The stability parameters of a drug dosage form can be influenced by environmental conditions of storage such as temperature, light, air and humidity as well as the package components (2). The importance of stability testing in the development of pharmaceutical dosage forms is well recognized in the pharmaceutical industry. Increased filings of ANDA (Abbreviated new drug applications), by generic and non-generic drug manufacturers have resulted in an increase in submissions of stability data to the FDA (food and drug administration).

The purpose of stability studies-study design (3) is based on the following phenomena. To gain a thorough understanding of any chemical and physical changes and microbiological changes to which drug substances and drug products may be exposed, during their life cycle under different storage conditions. To confirm that the drug substances and products are assured of their efficacy and safety in marketed packs, throughout the cycle of warehousing, distribution, storage and use. To recommend storage conditions, re-test periods and shelf life. To demonstrate the consistency and skill of production and packing of drug substances and/or drug product for quality, batch after batch, in a standard manufacturing process. To monitor any changes in manufacturing process and its impact on quality. Pack selected for stability studies should be the marketed / proposed to be marketed pack, or simulate the actual pack used for storage and distribution .If a product has more than one pack, stability studies should be carried out on each of the packs. Container closure evaluation should be for in-process storage, transportation of product, compatibility with packaging materials, moisture permeation, light exposure and closure seal ability. The parameters such as, tests for appearance, potency, moisture, color, odor, DT, dissolution, friability, hardness, dispersion time, preservatives and film adherence for the tablets (Coated and Uncoated) are selected for evaluation.

As a general guideline, the following principles should be taken into consideration in formulating tablet stability protocols (3, 4). Less stable tablet materials and formulas would require more frequent testing. The amount of testing required for an active or tablet product depends on the amount of data already available. Stability - indicating assay should be used for testing at the appropriate scheduled intervals. Tablets in final packing closure systems intended for marketing will be submitted to such tests. The scope and design of a stability study vary according to the product and the manufacturer concerned (5). Ordinarily the formulator of a product first determines the effects of temperature, light, air, pH, moisture, trace metals, and commonly used excipients or solvents on the active ingredient(s). From this information, one or more formulations of each dosage form are prepared, packaged in suitable conditions, both exaggerated and normal. Good manufacturing practice (GMP) requirements for drug stability (section 211.166 and 211.167) and expiration dating (section 211.137), and FDA guidelines for stability studies (section 98) contain significant and specific information related to conducting of stability studies and assigning expiration dates (6). International Conference on Harmonization of technical requirements for registration of pharmaceuticals for human use (1991) has developed more than 40 guidelines under 4 major heads. **Q** "Quality" topics i.e., those relating to chemical and pharmaceutical quality assurance (7). The globe had been dissected into four zones for stability testing. (7, 8, 9). Stability study storage conditions and testing frequencies are given in table1.

Table 1. Stability study storage conditions (10)

Stability study	Storage conditions	Testing frequency (Months)
Accelerated	40 ± 2°C & 75 ± 5% RH	0,1,2,3 & 6
Intermediate	30 ± 2°C & 65 ± 5% RH	0,3,6,9,12,18,24 & 36
Long term/RT	25 ± 2°C & 60 ± 5% RH	0,3,6,9,12,18,22,24,26,36,48 & 60

Since parent guideline Q1A (R2) brief in nature and limited in scope and provides a clear explanation of expectations when proposing a retest period or shelf life and storage conditions and outlines recommendations for establishing these from single or multi factor and full or reduced-design studies. However, LT and accelerated data show little or no change over time and little or no variability or amenable to statistical analysis the maximum shelf life period that can be assigned is given by: Shelf life Y = up to 2X months but not exceeding X + 12 months, where X is the period for which real temperature/long term data is submitted.

EXPERIMENTAL

Materials and Methods:
Amoxicillin and Potassium clavulanate tablets USP (875-125mg), the working standards of Amoxicillin and Pottasium clavulanate were obtained from APL Hyderabad, India. Methanol (HPLC grade) and other chemicals were procured from Merck, Ltd, Mumbai and S.D. fine chemicals Ltd, Mumbai respectively.

1. Estimation of Amoxicillin and clavulanate Potassium tablets by HPLC Method[5].
The assay of Amoxicillin and clavulanic acid was carried out using USP HPLC Method, Which is designated as stability indicating method because of its capability to distinguish the degraded product with parent one. The following table shows the chromatographic conditions.

Table 2. Sstimation of amoxicillin and clavulanate potassium tablets USP by high performance liquid chromatography (HPLC) method (6) chromatographic conditions.

Column	Flow rate	Detection	Column oven temp	Injection volume	Run time
Hypersil BDS C_{18}, 5µ (150 x 4.6 mm)	2.0 mL / min	UV, 220 nm	25°C	10 µl.	5 min.

2. Stability study:
Stability study as per ICH guidelines was carried out for the Amoxicillin and clavulanate Potassium tablets. The stability protocol is designed and shown in Tables 3, 4, 5,6,7,8

Table 3. . Stability study protocol and Product details.

Product name	Generic name	Label claim
Amoxicillin and Clavulanate Potassium Tablets USP 875–125 mg	Amoxicillin and Clavulanate Potassium Tablets USP 875–125 mg	Each film coated tablet contains: Amoxicillin trihydrate USP (equivalent to amoxicillin) – 875mg : Potassium clavulanate USP diluted with MCC (Avicel)(1 : 1) (equivalent to clavulanic acid) – 125 mg

Manufacturing date: May 2005.

Table 4. Packaging component details

Product presentation	**Container details**	**Closure details:** (Outer cap, Inner cap, Lining, Head seal)	**Molecular sieves** (Desiccant) – 2 no's
Amoxicillin and Clavulanate Potassium Tablets USP 875 – 125 mg packed in 20's count using HDPE containers	Material of construction – 100 CC High density poly ethylene (HDPE) Resin grade – MARLEX HHM5502BN Colorant – White 11078	Child resistant closure Material of construction – 38 mm with Tekni-plex induction seal pulp board coated with wax. Resin grade – Polypropylene Colorant – White ampacet	The samples were stored in different stability chambers as given in Table 5. Reference samples and working standards were stored at 4°C.

The sample testing intervals, number of containers to be discharged and the pharmaceuticals to be analyzed in tables 5 and 6.

Table.5. Storage Conditions as per ICH guidelines Q1A (10)

Storage condition	**Temperature**	**Relative Humidity**
Accelerated study	40 ± 2°C	75 ± 5 % RH
Long term/RT	25 ± 2°C	60 ± 5% RH

Table 6. Stability study Plan

S. No	**Test interval (months) [10]**		**No. of containers to be discharged**	**Parameters to be analyzed**
	Accelerated	**Long term**		
1	0	0	3	I
2	1	-	3	I
3	2	-	3	I
4	3	3	3+3	I, II
5	6	6	3+3	I, II

Table. 7. Parameters to be analysed

Category	**Tests**
I	Description, Average weight, Dissolution, Assay, Moisture content, Water activity
II	Dissolution Profile

Table 8. Acceptance criteria for the parameters tested (USP: Specifications)

Sl. No	TEST	SPECIFICATION
01	Description	White colored, capsule shaped, film coated tablet, debussed with "A" on one side and a score line in between '6' and '5' on the other side.
02	Average weight (mg)	1471.0 ± 3.0% (1426.87 – 1515.13)
03	Dissolution (By HPLC) Amoxicillin ($C_{16}H_{19}N_3O_5S$) Clavulanic acid ($C_8H_9NO_5$)	≥ 85 % (Q) of labeled amount of amoxicillin is dissolved in 30 min. ≥ 80 % (Q) of labeled amount of clavulanic acid is dissolved in 30 min.
04	Moisture content (% w/w, By KF)	≤ 11.0 %
05	Assay (By HPLC) Amoxicillin, in mg. % Labeled amount Clavulanic acid, in mg. % Labeled amount	787.50 – 1050.00 90.0 – 120.0 112.50 – 150.00 90.0 – 120.0
06	Water activity (%RH)	≤ 0.15

3. Dissolution study[5]:
The dissolution studies were carried out using the apparatus USP Type II (Paddle) with the RPM of 75 and the dissolution medium is 900 ml of water and the temperature 37±0.5°C was maintained. The dissolution study was done in two ways one is Dissolution profile study and another is Dissolution Q point study.

i) **Dissolution profile study:** Typically, the profile was measured by fixed timse point dissolution and techniques and calculations, except that the samples were taken at several time points.

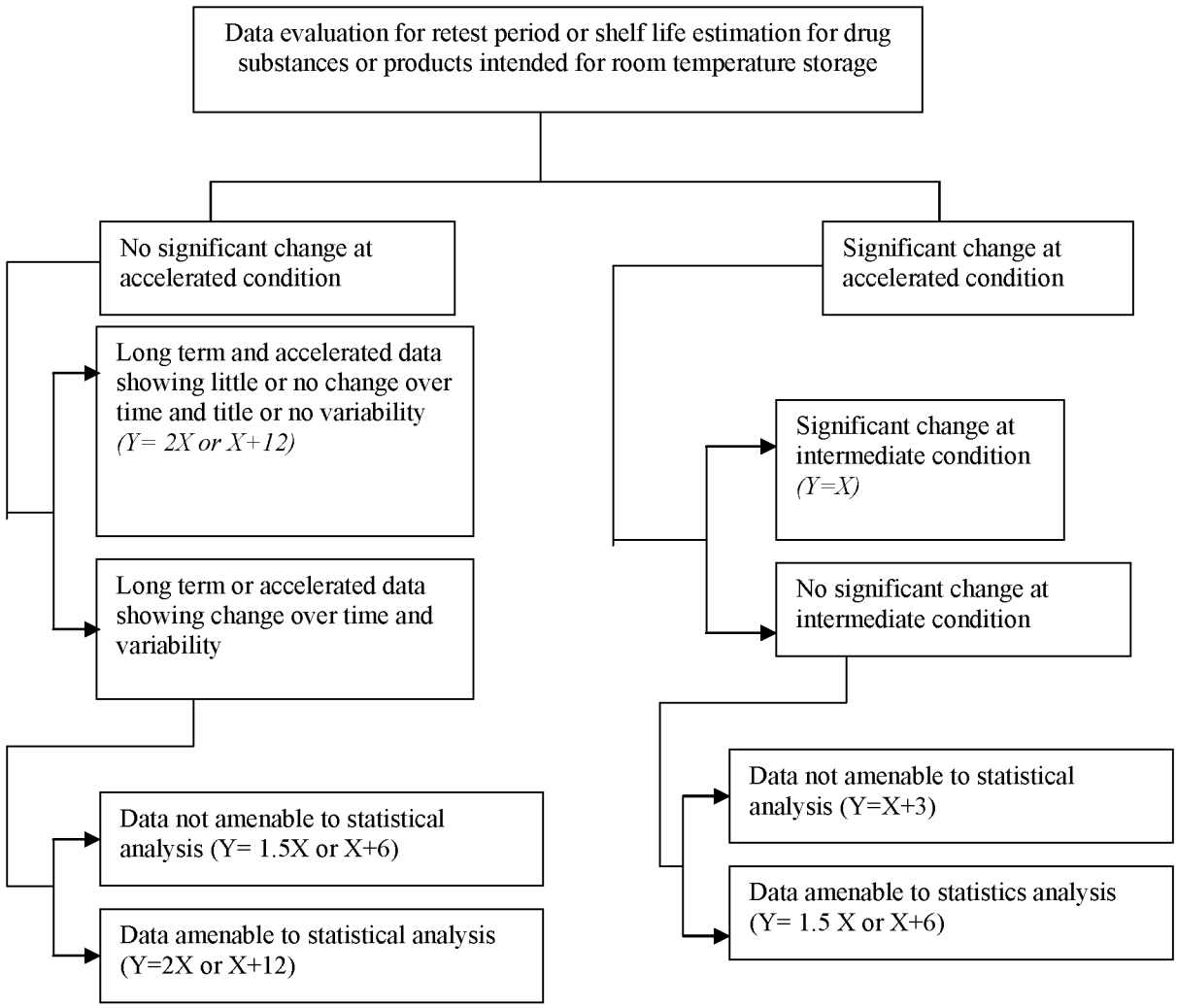
Procedure: The parameters of dissolution apparatus were set, added one tablet into each of six dissolution vessels. The dissolution apparatus was immediately started. 10mL of the sample solution was withdrawn at the end of 10, 20 and 30 minutes from each dissolution vessel, and replaced with 10mL of dissolution medium after each sample withdrawal. This solution was filtered through 0.45µ membrane filter, filled into vials and labeled appropriately.

ii) Dissolution "Q" point study:

Procedure: The parameters of dissolution apparatus were set, added one tablet into each of six dissolution vessels. The dissolution apparatus was immediately started. 10mL of the sample solution was withdrawn at the end of 30 minutes from each dissolution vessel. This solution was filtered through 0.45µ membrane filter, filled into vials and labeled appropriately.

4. Moisture content determination:
The moisture content was determined by Karl-Fisher apparatus and in the method 30ml of dried methanol was taken in KF apparatus beaker, and neutralized with fresh KF reagent. Accurately weighed quantity of powdered tablet has been transferred into the neutralized methanol present in the beaker. The titer value is noted.

Table 9. Decision tree for data evaluation for shelf life estimation of drug products (9, 11).



Key: Y: proposed retest period or shelf life: X: available long term stability data

RESULTS AND DISCUSSION

Amoxicillin and Potassium Clavulanate USP 875 -125mg tablets in the final package, HDPE bottles were tested for the analytical parameters such as description, average weight, moisture content, assay, dissolution profile study and water activity, at zero month as given in tables (7) and (8). The remaining sample containers were divided to get twice the number required to carry out the analysis at prescribed sampling intervals, to compensate any problems during the analysis.

After giving the first injection of standard solution, the chromatogram was processed and system suitability report was generated, in each case starting from zero to 6^{th} month. It was observed that the plate count for amoxicillin and clavulanic acid was found to be 2893.70 and 2725.44 respectively. The column efficiency was found to be more than 2500 theoretical plates for both the peaks; therefore the system was suitable and appropriate for further study, for the rest of the months. The % RSD for the peaks was found to be 0.3 and 0.2% which is with in the allowable limit of 2.0 %. The initial amount of amoxicillin and clavulanic acid was found to be 883.54 mg and 127.40 mg respectively. The % potency was found to be 100.98 and 101.92 for amoxicillin and clavulanic acid respectively. It was observed that the plate count for amoxicillin and clavulanic acid was found to be 3097.6 and 3123.6 respectively. For the second month, it was observed that the plate count for amoxicillin and clavulanic acid was found to be 3566.1 and 3799.3 respectively. For the third month, it was observed that the

plate count for amoxicillin and clavulanic acid was found to be 4143.5 and 4243.9 respectively. For the sixth month, it was observed that the plate count for amoxicillin and clavulanic acid was found to be 3229.6 and 2988.0 respectively. The % potency was found to be 98.44 and 100.02 for amoxicillin at accelerated and real temperature conditions respectively. The % potency was found to be 97.05 and 100.44 for clavulanic acid at accelerated and real temperature conditions respectively (Fig.1). The % potency versus Time graph reveals that there is an increased loss in drug content of amoxicillin and clavulanic acid at accelerated conditions compared to RT/LT conditions. The loss in potency of clavulanic acid is more compared to potency of amoxicillin. Though there is an increased loss in potency of clavulanic acid, it is considered to be insignificant, since the loss is < 5% (as per Q1A (R2) and USFDA) i.e., from 101.92 to 97.05 and 100.44 at accelerated and RT conditions respectively.

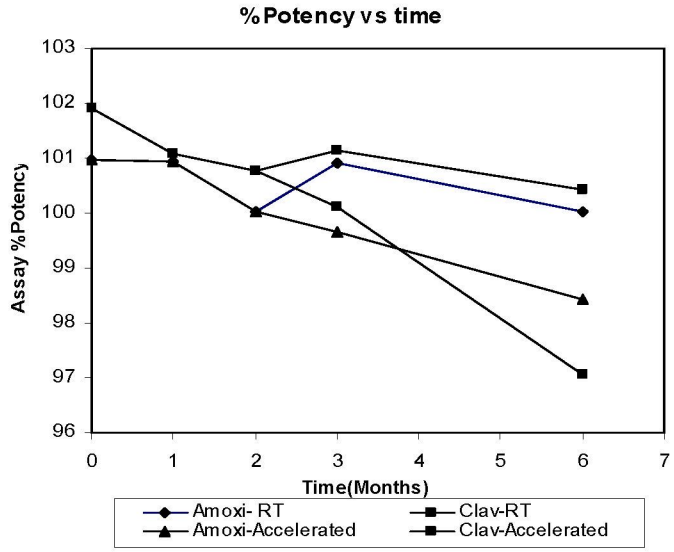
For the first month, it was observed that the plate count for amoxicillin and clavulanic acid was found to be 2751.1 and 3065.0 respectively. For the second month, it was observed that the plate count for Amoxicillin and Clavulanic acid was found to be 3389.3 and 3680.3 respectively. For the third month, it was observed that the plate count for amoxicillin and clavulanic acid was found to be 3389.3 and 3680.3 respectively. The % RSD for the peaks was found to be 0.1 and 1.1%, which is in the allowable limit of 2.0 %. For the sixth month, it was observed that the plate count for amoxicillin and clavulanic acid was found to be 3001.6 and 2866.3 respectively. The % RSD for the peaks was found to be 0.3 and 0.4%, which is with in the allowable limit of 2.0 %. It has been observed that the % drug release after 30 minutes was found to be 100.60 and 102.80 for amoxicillin and clavulanic acid respectively and the same is compared with zero month data. At accelerated conditions (40°C and 75% RH) 36 containers and at real temperature conditions (25°C and 60% RH) 24 containers were kept in respective stability chambers which were maintained at prescribed storage conditions as mentioned in the Table 4. As per ICH guidelines the precision in set conditions recommended at ± 2°C and ± 5% RH to the set temperature and humidity conditions. However, during the present study the precision control is set at ± 0.5°C and ± 2% RH so that the samples are subjected to more stringent temperature and humidity conditions. The samples were withdrawn at prescribed sampling intervals and analyzed for the said parameters as given in Tables 7 and 8 using the test procedures detailed in the chapter "Materials and Methods". The following are the results obtained, after the study. The results were given in a comparative way for accelerated and real temperature data as per testing intervals for each stability testing parameter as shown in the table 10.

The data (table 14 and 15) was subjected to one way ANOVA – Design 1 between subject factor using ezANOVA statistical package. Pairwise comparisions yielded the $p < 0.05$ which clearly indicated not significant with very small standard deviation values.

Table 10. Summary table for assay

Test interval (Months)		AMOXICILLIN		CLAVULANIC ACID	
		Labeled amount (mg)	% Potency	Labeled amount (mg)	% Potency
Zero month		883.54	100.98	127.40	101.92
1st month		883.16	100.93	126.36	101.09
2nd month		875.29	100.03	125.97	100.78
3rd month	Accelerated	872.05	99.66	125.14	100.11
	RT/LT	883.09	100.92	126.44	101.15
6th month	Accelerated	861.36	98.44	121.31	97.05
	RT/LT	875.21	100.02	125.55	100.44

Figure 1. % Potency vs time



The dissolution studies were carried out for the specified time intervals to study the effect of accelerated temperature and humidity on the % drug release from the tablets. The dissolution studies were carried out as

(i) Dissolution profile study up to 30 minutes at an interval of 10 minutes and

(ii) Dissolution 'Q' point study at the end of 30 minutes.

The results of the dissolution study indicate that there is no significant change in % drug release as shown in Fig. 2a, Fig. 2b, Fig. 3a and Fig. 3b.

Figure 2a. Comparative DPs for zero month and 3rd month accelerated data

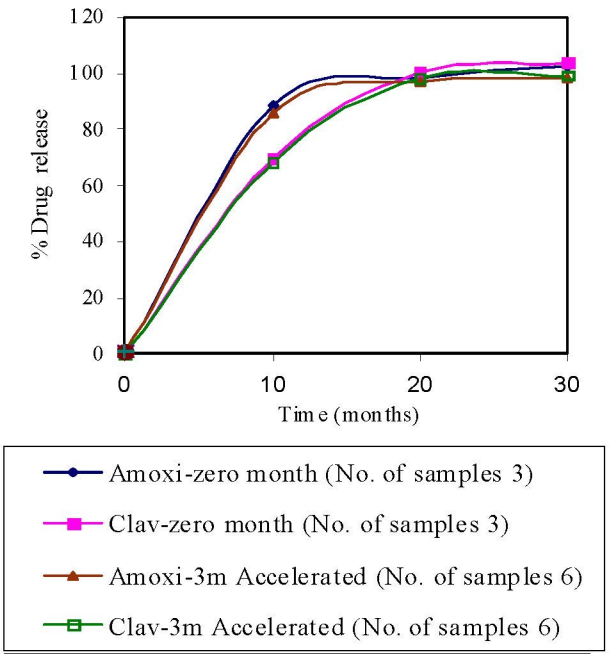


Figure 2b. Comparative DPs for zero month and 6rd month accelerated data

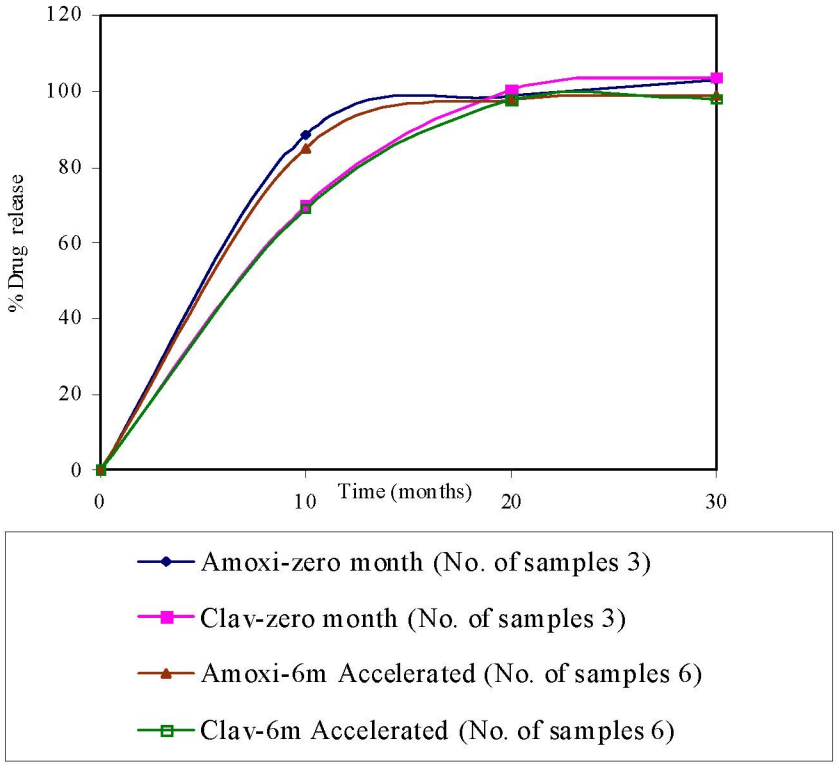


Figure 3a. Comparative DPs for zero month and 3rd month RT data

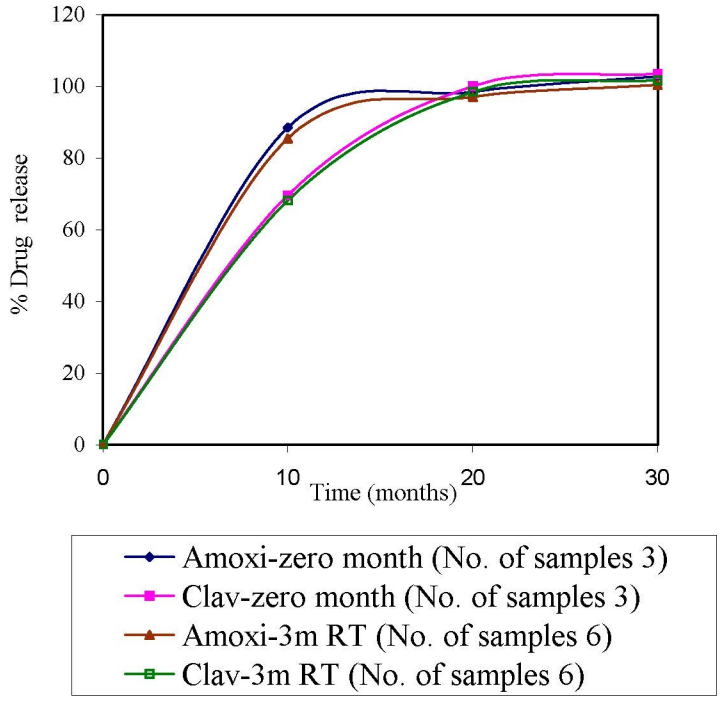


Figure 3b. Comparative DPs for zero month and 6rd month RT data

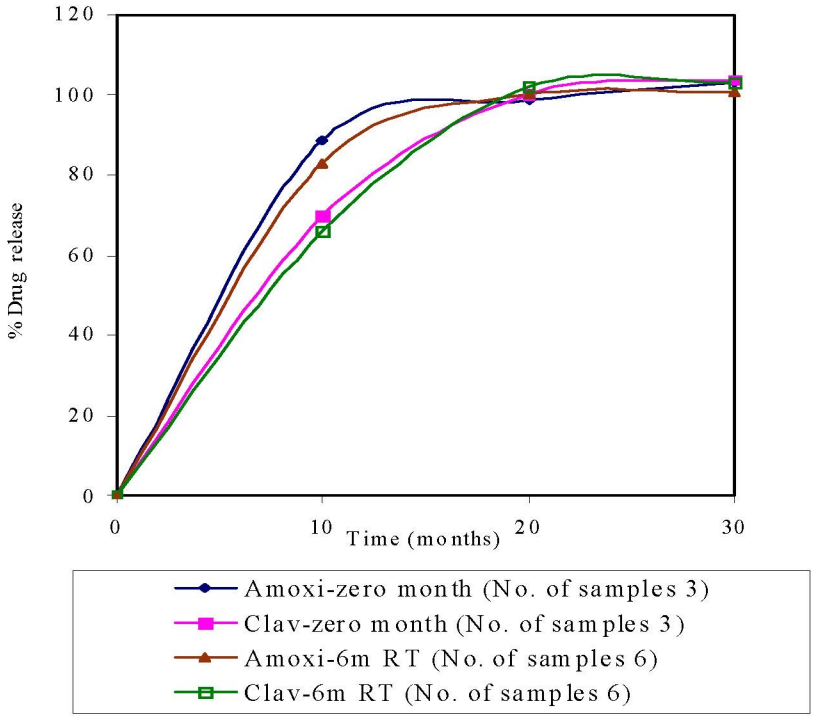


Table 11, Retention times at zero & 6th months

S.No.	Description	Peak Name	Retention times(min)
1.	Assay – Standard chromatograms for zero months	i) clavulanic acid ii) Amoxcillin	1.486 2.384
2.	Assay – sample chromatography for zero month	i) clavulanic acid ii) Amoxcillin	1.487 2.387
3.	Assay – standard chromatograms for 6th month	i) clavulanic acid ii) Amoxcillin	1.663 2.740
4.	Assay – sample chromatograms for 6th months – accelerated conditions	i) clavulanic acid ii) Amoxcillin	1.664 2.742

Table 12. Accelerated stability data of amoxicillin and potassium clavulanate tablets USP 875/125 mg

PRODUCT NAME	**:**	**Amoxicillin and Clavulanate Potassium Tablets USP 875/125 mg**	BATCH TYPE	:	PIVOTAL BATCH
BATCH NO.	:	Project	BATCH SIZE	:	5000 Tablets
MFG.	:	05 / 2005	**STORAGE CONDITION**	**:**	**40° C ± 2° C / 75% RH ± 5% RH**
EXP.	:	-	PACK DETAILS	:	100cc HDPE Container of 20's Count with Child Resistant Closure with Induction heat seal
DRUG PRODUCT MFG. LOCATION	:	Aurobindo Pharma Ltd., Hyderabad (Unit XII)	CONTAINER DETAILS	:	100 cc HDPE Container
	:		CLOSURE DETAILS	:	Child Resistant Closure 38 mm with Tekni-plex Induction Seal

Station	Date of Analysis	Description	Assay (By HPLC)		Dissolution (By HPLC)		Water (By KF)	Water Activity
			Amoxicillin USP as Amoxicillin anhydrous	Clavulanic acid	Amoxicillin USP as Amoxicillin anhydrous	Clavulanic acid		
Specification		White colored, capsule shaped, film coated tablets debossed with "A" on one side and with a score line in between '6' and '5' on the other side.	787.50 – 1050.00 mg (90.0 – 120.0 % w/w)	112.50-150.00 mg (90.0-120.0 % w/w)	NLT 85% (Q) of the labeled amount of Amoxicillin is dissolved in 30 minutes.	NLT 80% (Q) of the labeled amount of Clavulanic acid is dissolved in 30 minutes.	NMT 11.0% w/w	NMT 0.15%
Initial	07/28/2005	White colored, capsule shaped, film coated tablets debossed with "A" on one side and with a score line in between '6' and '5' on the other side	883.54 mg (100.98%)	127.40 mg (101.92 %)	1) 100.98 2) 103.37 3) 103.54 4)102.86 5) 102.86 6) 103.04 Mean: 102.78±0.923*	1) 102.05 2) 104.45 3) 104.22 4) 103.39 5) 103.72 6) 103.56 Mean: 103.56±0.939*	5.95%	0.04
1st month	08/28/2005	White colored, capsule shaped, film coated tablets debossed with "A" on one side and with a score line in between '6' and '5' on the other side	883.16 mg (100.93%)	126.36 mg (101.09 %)	1) 100.76 2) 100.07 3) 100.79 4) 100.77 5) 100.63 6) 100.59 Mean:100.60±0.273*	1) 101.02 2) 100.30 3) 100.97 4) 100.93 5) 100.83 6) 100.59 Mean: 100.77±0.277*	6.41%	0.06
2nd month	09/29/2005	White colored, capsule shaped, film coated tablets debossed with "A" on one side and with a score line in between '6' and '5' on the other side	875.29 mg (100.03%)	125.97 mg (100.78 %)	1) 99.46 2) 98.87 3) 101.38 4) 101.39 5) 101.21 6) 101.42 Mean: 100.62±1.146*	1) 99.95 2) 99.79 3) 100.40 4) 100.56 5) 100.33 6) 100.38 Mean:100.24±0.297*	7.28%	0.06
3rd month	10/28/2005	White colored, capsule shaped, film coated tablets debossed with "A" on one side and with a score line in between '6' and '5' on the other side	872.05 mg (99.66%)	125.14 mg (100.11%)	1) 98.32 2) 98.39 3) 98.67 4) 98.71 5) 98.44 6) 98.57 Mean: 98.52±0.158*	1) 98.75 2) 99.29 3) 99.31 4) 99.66 5) 99.16 6) 99.47 Mean: 99.27±0.309*	8.16%	0.08
6th month	01/28/2006	White colored, capsule shaped, film coated tablets debossed with "A" on one side and with a score li ne in between '6' and '5' on the other side	861.36 mg (98.44%)	121.31 mg (97.05%)	1) 98.75 2) 98.47 3) 99.07 4) 98.68 5) 98.20 6) 98.07 Mean: 98.54±0.370*	1) 97.98 2) 97.89 3) 98.36 4) 98.29 5) 97.51 6) 97.73 Mean: 97.96±0.325*	9.09%	0.1

Table 13. Long term stability data of amoxicillin and potassium clavulanate tablets USP 875/125 mg (for 6 months)

PRODUCT NAME	**:**	**Amoxicillin and Clavulanate Potassium Tablets USP 875/125 mg**		BATCH TYPE	:	PIVOTAL BATCH
BATCH NO.	:	Project		BATCH SIZE	:	5000 Tablets
MFG.	:	05 / 2005		**STORAGE CONDITION**	**:**	**25°C ± 2°C / 60% RH ± 5% RH**
EXP.	:	-		PACK DETAILS	:	100cc HDPE Container of 20's Count with Child Resistant Closure with Induction heat seal
DRUG PRODUCT MFG. LOCATION	:	Aurobindo Pharma Ltd., Hyderabad (Unit XII)		CONTAINER DETAILS	:	100 cc HDPE Container
	:			CLOSURE DETAILS	:	Child Resistant Closure 38 mm with Tekni-plex Induction Seal

Station	Date of Analysis	Description	Assay (By HPLC)		Dissolution (By HPLC)		Water (By KF)	Water Activity
			Amoxicillin USP as Amoxicillin anhydrous	Clavulanic acid	Amoxicillin USP as Amoxicillin anhydrous	Clavulanic acid		
Specification		White colored, capsule shaped, film coated tablets debossed with "A" on one side and with a score line in between '6' and '5' on the other side.	787.50 – 1050.00 mg (90.0 – 120.0 % w/w)	112.50-150.00 mg (90.0-120.0 % w/w)	NLT 85% (Q) of the labeled amount of Amoxicillin is dissolved in 30 minutes.	NLT 80% (Q) of the labeled amount of Clavulanic acid is dissolved in 30 minutes.	NMT 11.0% w/w	NMT 0.15%
Initial	07/28/2005	White colored, capsule shaped, film coated tablets debossed with "A" on one side and with a score line in between '6' and '5' on the other side	883.54 mg (100.98%)	127.40 mg (101.92 %)	1) 100.98 2) 103.37 3) 103.54 4)102.86 5) 102.86 6) 103.04 Mean: 102.78 ± 0.922*	1) 102.05 2) 104.45 3) 104.22 4) 103.39 5) 103.72 6) 103.56 Mean: 103.56 ± 0.844*	5.95%	0.04
3rd month	10/28/2005	White colored, capsule shaped, film coated tablets debossed with "A" on one side and with a score line in between '6' and '5' on the other side	883.09 mg (100.92%)	126.44 mg (101.15%)	1) 101.21 2) 99.92 3) 100.64 4) 99.87 5) 99.64 6) 101.39 Mean: 100.44 ± 0.744*	1) 102.31 2) 101.26 3) 101.07 4) 101.73 5) 101.14 6) 102.79 Mean: 101.72 ± 0.702*	6.57%	0.05
6th month	01/28/2006	White colored, capsule shaped, film coated tablets debossed with "A" on one side and with a score line in between '6' and '5' on the other side	875.21 mg (100.02%)	125.55 mg (100.44%)	1) 100.12 2) 100.11 3) 101.01 4) 100.46 5) 101.09 6) 100.80 Mean: 100.60 ± 0.433*	1) 101.57 2) 102.05 3) 103.22 4) 103.18 5) 103.41 6) 103.53 Mean: 102.83 ± 0.822*	6.85%	0.06

CONCLUSION

Stability evaluation of amoxicillin and clavulanate potassium tablets was performed as per ICH guidelines QIA (R2) by analyzing various parameters such as description, assay, dissolution, water content, water activity and shelf life at zero, 1st, 2nd, 3rd and 6th month intervals at room temperature (25°C±2°C/ 60% RH ± 5% RH) and accelerated conditions (40°C ± 2°C / 75% RH ± 5% RH). All the parameters do not found to be changed significantly over a study period (6 months). The shelf life of the tablets was found to be 48.2 months by the linear regression analysis of the stability data generated. In view of the results obtained that amoxicillin and clavulanate tablets tested are recommended to be stored at 25°C and the stability of the tablets confirmed the ICH & USFDA guidelines.

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