THE INFLUENCE OF STORAGE PATTERNS ON THE STABILITY OF PARACETAMOL SYRUP CONCENTRATION

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Abstract

The aim of this research is to study the influence of storage patterns on the stability of paracetamol syrup patent concentration. Paracetamol syrup was taken from one of patent product that taken in Malang,in the same batch of 6 bottles. Research done by given special treatment to the sample, stored at refrigerator and room temperature. Number of Paracetamol concentrations in the samples was measured every week by aid of HPLC (High Performance Liquid Chromatography) equipped 243 nm detector and 3.5 mm X 30cm column containing fillers, and flow rate approximately 1.5 ml per minute. Results : The concentration of active ingredient Paracetamol syrup (patent) that stored at refrigerator temperature at week-6 =94,29% and at room temperature = 94,5%. Conclusion : Paracetamol syrup patent (Brand X) still feasible for use in timeframe of 6 weeks after first time used due still comply the requirements of Indonesian Pharmacopeia IV Ed, is not less than 90% and not more than 110%.

Key words : *Paracetamol, Stability, Storage Patterns, HPLC*

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INTRODUCTION

For fever (antipyretic) in children who are recommended by WHO since 1997 until now is Paracetamol. Because paracetamol is relatively safer than other antipyretic drugs to children. In the high dose is about 10g/hari (200-250mg/kgBB) Paracetamol hepatotoxicity have side effects or impaired liver function, liver and liver. However, if used at therapeutic dose range is still safe . Stability is the ability of a drug product to maintain the properties and characteristic.are so similar to those owned at the time made include the identity, strength, quality, purity within the limits established during the period of storage and use (Lachman, Lieberman, 1994).

Stability of paracetamol solution is not stable to light so that should be protected from light, in the dry state paracetamol stable at temperatures up to 45 ? C. Hydrolysis product p-aminophenol paracetamol act as a contaminant or as an end result which shows the degradation of p-aminophenol with oxidation mechanisms of quinonimine and coloring products to pink, brown and black. Paracetamol is relatively stable to oxidation (Anonymous, 1994) or the levels of degradation products are not efficacious, are toxic, so it becomes unsafe . Formulation of the problem is there a pattern of influence of storage on the stability of paracetamol syrup levels of patent.

RESEARCH METHODOLOGY

The design of the study this study is an experimental study of the stability of the storage time of paracetamol in syrup stored in the refrigerator temperature and room temperature. Dependent variable used is the time variable, and the independent variables are the levels. Assay of paracetamol

A. Mobile phase Create a water-methanol mixture of P (3:1), filtered

B. Standard solution .Standar 1: carefully weighed ± 100 mg paracetamol and incorporated into 100.0 ml volumetric flask, added aquabidest to mark the line, shake homogeneous. So we get the raw content of 1000 ppm for paracetamol.

Pipetted 2.0 ml of raw stem 1, is inserted into a 50.0 ml volumetric flask, added aquabidest to mark the line, shake homogeneous. So we get the raw content of 40ppm for paracetamol.

C. Working standard solution

Standard 1: pipetted 5.0 ml of raw stem 2, dissolved in mobile phase to mark the line, shake homogeneous. So we get the raw content of the work 4ppm.

Standard 2: pipetted 5.0 ml of raw stem 2, dissolved in mobile phase to mark the line, shake homogeneous. So we get the raw content of 8ppm work.

Standard 3: pipetted 0.5 ml of raw stem 1, dissolved in mobile phase to mark the line, shake homogeneous. So we get the raw content of 10ppm standard 4: pipetted 3.0 ml of raw stem 2, dissolved in mobile phase to mark the line, shake homogeneous. So we get the raw content of 12ppm

Standard 5: 10.0 ml pipetted raw stem 2, dissolved in mobile phase to mark the line, shake homogeneous. So we get the raw content of 16ppm work.

D. Test solution

Measure carefully the solution of paracetamol syrup as much as 1.0 ml, introduced into 25.0 ml volumetric flask, added aquabidest to mark the line, shake homogeneous solution thus obtained to test levels of 960 ppm.

Pipette solution of the above as much as 1.0 ml, put in a 10.0 ml volumetric flask, added aquabidest to mark the line, shake homogeneous solution thus obtained to test levels of 96 ppm.

Pipette solution of the above as much as 1.0 ml, put into 10.0 ml volumetric flask, add the mobile phase to mark the line, so we get whipped homogeneous levels of 9.6 ppm for the test solution.

Chromatographic systems and procedures High performance liquid chromatography equipped with a 243 nm detector and a column 3.5 mm x 30 cm containing fillers L1. The flow rate of approximately 1.5 ml per minute. Perform chromatography of standard solution, record the peak responses shown in Procedure: the column efficiency is not less than 1000 theoretical plates, follow no more than a factor of 2 and the relative standard deviation on repeated injections. Inject separately equal number of volumes (approximately 10 ml) of standard solution and test solution into the chromatograph, the main peak of the response measure. Calculate the amount in mg of C8H9NO2, in each ml of oral solution.

Paracetamol syrup levels in the calculation is done using the regression line equation of the standard curve, the relationship between levels and chromatogram peak area of paracetamol: y = bx + a. Obtained from these calculations in units of ppm levels of paracetamol, then converted into the number mg/5ml; to match the label on sanmol syrup preparations, using the following calculation:

The formula x samples: 5mg / X x 100ml samples of testing levels

Research instruments

The instrument used for the assay of paracetamol syrup is a high performance liquid chromatography (HPLC)

Data collection methods

The method used to answer the formulation of the problem is to compare test results with the levels of paracetamol syrup provisions contained in the fourth edition of the Pharmacopoeia Indonesia, "paracetamol oral solutions containing paracetamol, not less than 90% and not more than 110% of the amount stated on the label ", where if the levels are obtained to meet the provisions stated storage stable, otherwise if it does not meet the provisions of the fourth edition of the Pharmacopoeia Indonesia declared volatile storage.

Data was collected through the following stages:

Assays performed on all the good paracetamol syrup stored at room temperature or refrigerator temperature, the period May-July 2011.

Recapitulated in the tables includes:

Sampling time of test in Refrigerator temperature and Room temperature.

Analysis of the data content of paracetamol in syrup

Effect of storage described descriptively according to the pattern seen in the curve pattern vs paracetamol content of the storage time

RESULTS

Determination of Levels of paracetamol syrup Paracetamol syrup levels determined by using HPLC method. Beginning with the creation of standard solution and then measured the peak area of paracetamol both chromatograms of standard solution or sample solution.Standard curve data. Standard area of measurement results correlated with the levels and the results of the regression equation shown in table I

Table I. Parameters of regression equation of standard curve

Week	Correlation coeffisient	SLOPE	INTERCEPT
0.	0,9972	70.045,14	17.229,9
1.	0,9999	70.565,31	1,639
2.	0,9996	74.049,62	-17.927
3.	0,9998	74.829,6	-5.881
4.	0,9996	72.008,6	8.495
5.	0,9997	73.383,8	-1.274

Data measured levels of paracetamol syrup sample patents (Brand X).

The results of measurements of levels in ppm converted to mg / ml to match the label listed on the patent Paracetamol syrup samples (Brand X)

Table II. Levels of paracetamol syrup sample patents (Brand X) The Stored in the fridge temperature (4 ° C)

Week	Bottle 1 (mg)	bottle 2 (mg)	bottle 3 (mg)	average (mg)
0.	27.27	27.8	24.5	26.52
1.	22.76	22.8	23.94	23.16
2.	22.74	23.25	23.37	23.12
3.	22.62	22.32	22.42	22.45
4.	24.35	23.32	23.72	23.79
5.	23.075	22.22	22.27	22.53
6.	22.37	22.8	22.72	22.63

Table III. Levels of paracetamol syrup sample patents (Brand X) The stored at room temperature (26 ° C)

Week	Bottle 1 (mg)	bottle 2 (mg)	bottle 3 (mg)	average (mg)
0.	24.57	23.67	23.57	23.93
1.	24.35	23.27	23.4	23.67
2.	27.025	22.55	22.62	24.06
3.	22.32	22.42	22.5	22.41
4.	23.15	22.42	23.65	23.07
5.	22.17	22.42	22	22.19
6.	22.67	22.75	22.62	22.68

Calculation

The calculation of ppm to mg 5ml/125mg sample label and in the pipette 1ml (1ml/5ml x 125 mg = 24 mg), means in a 1 ml sample pemipetan patent paracetamol syrup (Brand X) containing 24 mg paracetamol.

a. For weeks the temperature of the refrigerator

Bottle 1: 10.91 ppm. pipetted 1ml: 10.0 ml / 1.0 ml x 10.91 ppm = 109.1 ppm (L1), then L1 in pipette 1ml 10ml ad: 10.0 ml / 1.0 ml x 109.1 ppm = 1091 ppm (L2) and L2 in the pipette 1.0 ml ad 25.0 ml made in the form mg/1000 mg = 25 ml x 1091 mg = 27.27 mg.

Mg% for the calculation of the temperature of the refrigerator.

Calculation mg to % for refrigerator temperature

Week	Concentration	Concentration
0	26,52/24mg x 100%	110.5%
1	23,16/24mg x 100%	96.5%
2	23,12/24mg x 100%	96.33%
3	22,45/24mg x 100%	93.54%
4	23,49/24mg x 100%	97.87%
5	22,53/24mg x 100%	93.87%
6	22,63/24mg x 100%	94.29%

Calculation mg ke % for room temperature

Week	Concentration	Concentration
0	23,93/24mg x 100%	99,70%
1	23,67/24mg x 100%	98,62%
2	24,06/24mg x 100%	100,25%
3	22,41/24mg x 100%	93,37%
4	23,07/24mg x 100%	96,12%
5	22,19/24mg x 100%	92,45%
6	22,68/24mg x 100%	94,5%

Has done work Paracetamol assay standard in powder form to be used for quantitative analysis as well as paracetamol syrup samples using HPLC method. Using a reverse phase column (RP), at a wavelength of 243 nm. This wavelength is used as Paracetamol has a maximum absorption at a wavelength of 243 nm, so that the resulting error will be smaller.

In this study used a sample patent paracetamol syrup (Brand X) for 6 bottles, of which 3 bottles are stored in the fridge

temperature and 3 bottles stored at room temperature.

The next stage is the selection of mobile phase composition performed to obtain the appropriate polarity so as to separate paracetamol syrup with the matrix and to ensure optimal stain or analyte chromatogram peaks do not interfere with other substances. Selection of mobile phase was taken from the pharmacopoeia Indonesia (FI), which is water-methanol mixture with a ratio of 3:1 and flow rate used 1ml/menit.

Standard measurements performed at levels 4,8,10,12,16 ppm. At a wavelength of 243 nm and the measurement results obtained from the coefficient of variation for the week-0: a; 17229.9, b; 70045.14, r; 0.9972. Week-1: a; 1639.65, b; 70565.30, r; 0.9999. Week 2: a; -17 927, b; 74049.62, r; 0.9996. Week 3: a; -5881.8, b; 74829.6, r; 0.9998. Week 4: a; 8495, b; 72008.6, r; 0.9996. Week 5: a; -1274.4, b; 73383.8, r; 0.9997. Week-6: a; 19 293, b; 72042.8, r; 0.9998. Of raw measurements at week 0 to week-6 obtained values of r greater than 0.98 so that all the linear regression equation.

Samples measured at levels of about 24mg. And performed three times each replication of each bottle, the syrup obtained contains the active ingredient Paracetamol to-6 weeks at refrigerator temperature of 22.63 mg and 22.68 mg to room temperature. Then the unit was changed to a percent in order as stated in the Pharmacopoeia Indonesia, ED IV.

Paracetamol syrup obtained percent of its patent (Brand X) refrigerator for 94.29% and 94.5% for room temperature. Under the terms of issue of the pharmacopoeia Indonesia IV paracetamol oral solutions containing paracetamol are not less than 90% and not more than 110% of the amount listed on the label. Thus the results of measurements of samples at week-6 compliant Indonesian Pharmacopoeia IV.

CONCLUSION

The concentration of active ingredient Paracetamol syrup (patent) that stored at refrigerator temperature at week-6 =94,29% and at room temperature = 94,5%. Conclusion : Paracetamol syrup patent (Brand X) still feasible for use in timeframe of 6 weeks after first time used due still comply the requirements of Indonesian Pharmacopeia IV Ed, is not less than 90% and not more than 110%.

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