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Quantitative Analysis of Luliconazole by Using UV-Spectroscopy Bulk and Formulations

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ABSTRACT: Following paper include the development of economical quantitative method Luliconazole. Luliconazole trade name is LUZU. The UV method are developed using the methanol. absorbance (λ max) are archive at the 297nm and the celebration curve is plotted by using different dilution stock solution of the bulk and marketed formulation (cream, optimus pharma Pvt. Ltd.). And the validation parameters precision,accuracy, limit of detection, accuracy, limit of quantification. all the procedure is performed as per ICH guidelines. Linearity was found to be in range of 0.2-1.0 µg/ml with R^2 value 0.9934. the economical method of Luliconazole for quantitative analysis was developed by using Uv-spectroscopy. It is an imidazole antifungal medication. It is indicated for the treatment of athlete'sfoot, jock itch and ringworm caused by dermatophytes such as Trichophyton rub burn, MicrosPorum gypseum and Epidermophyton floccosum.

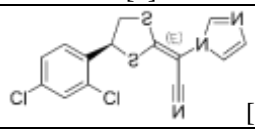
Keyword: absorbance, antifungal, quantitative analysis, UV-spectroscopy

I. INTRODUCTION: -

Luliconazole is as antifungal drug belong to class of dichlorobenzene class. is contained the bored spectrum of antifungal activity and is very potent against dermatophytes. IUPC name of the Luliconazoleis the (2E)-2- [(4R)-4-(2, 4-dichlorophenyl)-1, 3-dithiolan-2-ylidene]-2-imidazol-1-yl-acetonitrile. A molecular weight it 354.27 $g \cdot mol^{-1}$ [4] and the chemical formula is $C_{14}H_9Cl_2N_3S_2$. FDA approves this drug in to 2013[6].LUZU act by Inhibition CYCS P450 2C19[2]. It is also found that Luliconazoleis inhibit the enzyme Lanosterol demethylase which is essential for the synthesis of Ergosterol. Ergosterol is possess major part of the cell membrane of the fungi[4].

Drug profile of the Luliconazole:

Drug profile

IUPAC	(2E)-[(4R)-4-(2,4-Dichlorophenyl)-1,3-dithiolan-2-ylidene](1H-imidazol-1-yl)acetonitrile[4]
Formula:	$C_{14}H_9Cl_2N_3S_2$
Molar Mass:	354.27 $g \cdot mol^{-1}$[5]
MELTING POINT	150-154'C
Class of drug	imidazole Antifungal Medication[5]
Structure :	 [6]
appearance	yellow to yellow solid

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solubility	methanol: freely soluble acetone: freely soluble
mechanism of actions	o inhibit ergosterol synthesis by inhibiting the enzyme lanosterol demethylase
Absorption	Although Luliconazole is administered topically, clinical studies have shown that after the first dose in patients with tina pedis, a maximum plasma concentration of 0.40 ± 0.76 ng/mL (mean ± SD) occurred in 16.9 ± 9.39 hours (mean ± SD)[6].
distribution	yet to be determined. [6]
metabolism	elimination of Luliconazole has yet to be determined.[6]
log p	4.27[4]
Pka	6.34(strongest basic)[4]

II. MATERIALS AND METHOD:

1.1. Material:the API of the Luliconazolewe get as gift sample from the CENTURION LABORATORIES PVT LTD. pharmaceutical dosage form (cream, Optimus pharma Pvt. Ltd.) containing 1% w/w of Luliconazole was procured from local pharmacy.

Composition of cream

Composition (unison pharmaceutical PVT. LTD)	
Luliconazole	**1% w/w**
Preservative	
Benzyl Alcohol IP	**1% w/w**
Cream base	**q.s.**

1.2. Instruments:U.V Visible Spectrophotometer.

1.3. METHOD

1.3.1. Melting Point Determination: Melting Point of Luliconazole were determined by open capillary method using melting point apparatus in which the API was filled in one capillary tubes and were put in the melting point apparatus which show the melting range of the Luliconazole.

1.3.2. Method for checking solubility: The solubility was determined by taking of drug in 100ml volumetric flask and adding drop by drop0.1mili liter(ml) solvents at room temperature and shaking for few minutes. Solvents was added until drug dissolved completely. Solubility was measured by the required solvent quantity.

1.3.3. extractionof drug:10mili gram(mg) of cream base was taken in a 100mili litter(ml) volumetric flask, methanol was added until, the drug was dissolved by constant stirring and after complete dissolving of cream base the remaining volume was made up with methanol. This solution is filtered and from the filtrate suitable aliquots were diluted with methanol.

1.4. UV SPECTROSCOPY method for Luliconazole

1.4.1. Preparation of stock solutions: Accurately weigh quantity of 0.1mili gram(mg) of Luliconazoleand was transfer in to 100mili lilted(ml)volumetric flask, dissolved and diluted up to mark with methanol. It gives a stock solution having strength of 100µg/ml and 1000µg/ml.

1.4.2. Preparation of the sample solution: From stock solution accurately measured solution of Luliconazole(0.2,0.4,0.6,0.8,1ml) where

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transferred to 10ml volumetric flask make up to mark.

1.4.3. Selection of wavelength: Standard solution Luliconazolewere scanned overs the range of 200- 400nm but, selected wavelength of Luliconazole at 297nm so, drug detected at 297nm[4].

1.5. METHOD OF VALIDATION [9,8]

1.5.1. Linearity: The linearity determined by taking calibration curve of LuliconazoleAPL (0.2-1.0µg/ml) and marketing formulation (0.2-1.0 µg/ml) data are depicted in table [9].

1.5.2. Precision: Precision is the measure of the degree of repeatability of an analytical method under normal operation and is normally expressed as the percentage relative standard deviation for a statistically significant number of samples. According to the ICH, precision should be performed at three different levels: repeatability, intermediate precision, and reproducibility[9].

1.5.3. Range: The range of analytical procedure is the interval between the upper and lower concentration of analyse in the sample for which it has been demonstrated that the analytical procedure has a suitable level of precision, accuracy and linearity. Drug and separately weighed synthetic mixture. Measurement of response and plot response vs. concentration of analyse and demonstration of linearity by visual inspection of plot or appropriate statistical method[9].

1.5.4. Detection limit: The detection limit of an individual analytical procedures is the lowest amount of analyte in sample, which can be detected but not necessarily quantitated understated experimental conditions.it can be find out by visual evaluation, based on S/N ration applicable to procedure, which exhibit baseline noise, actual lowest concentration of analyte detected in compared with blank response or based on S.D of response and slope LOD [9].

$$LOD= 3.3*\sigma/s$$

Where, s =is slope of calibration curve, σ= S.D. of calibration curve

1.5.5. Quantitation limit: The quantitation limit of an individual analytical procedure is defined as the lowest amount of analyte in a sample, which can be quantitatively determined with suitable precision and accuracy. It can be find out by visual evaluation, based on S/N ration applicable to procedure, which exhibit baseline noise, actual lowest concentration of analyse detected in compared with blank response or based on S.D of response and slope LOQ [9].

$$LOQ= 10*\sigma/s$$

Where, s =is slope of calibration curve, σ= S.D. of calibration curve

1.5.6. Robustness: The robustness of an analytical procedure is a measure of it capacity to remain unaffected by small, but deliberate variations in method parameter and provide an indication of its reliability during normal usage. It should show the reliability of an analysis with respect to deliberate variations in method parameters. In case of the uvproctoscopy typical variations influence of analysis speed, wavelength [9].

1.5.7. Accuracy: Accuracy is measured as the percentage of analyse recovered by assay, by spiking samples in a blind study. Procedure is applied to analyse synthetic mixture of known purity.it calculated by taking minimum of nine determine means 3 replicate of medium concentration [8]

III. RESULTS AND DISCUSSION:

An attempt was made to develop simple and economical methods for the quantification of Luliconazole in pharmaceutical formulation and BLUK

1.6. Melting point determination:

Result of melting point

DRUG	REPORTED M.P	OBSERVATIONS M.P.
LULICONAZOLE	150-154	151-153

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1.7. Solubility study: the drug about the .5mg are dissolve in the following solution to determine the solubility in the different solvents and solubility study presents in table Ⅳ.

Result of solubility study

METHANOL	Freely soluble
Acetone	Freely soluble
0.1N HCL	Insoluble
0.1N NaOH	Insoluble
Diethyl ether	Sparingly soluble
Distilled Water	Sparingly soluble

Ⅳ

1.8. Spectral characteristics:spectrum of method areobtaining at 297 nm (λ max)for the stand test solution in methanol.

Spectral Characteristics.

Parameter	**Method**
λ max, nm	297nm
Beer's law limit	.2-1.0 µg/ml
Molar absorptivity (L/ mol/cm)	$4.1*10^{21}$l
Limit of detection	.421
Limit of quantification	1.27
Regression equation	Intercept (a) = 0.018 7
	Slope(b) =0.0414
	Correlation coefficient (r)= 0.9934
Y = a + bX, where Y is the absorbance, a is the intercept, b is the slope and X is the concentration in µg/ml	

1.9. Linearity: a linearity of the drug is found by the plotting the celebration curve between absorbance at λ max 297nm these regression equation is Y= abs (where Y= absorbance of drug, a= intercept, b=slop and X= concentration. A p lot was constructed by concentration on x-axis and absorbance on Y-axis and the correlation coefficient (r) was found to be .9934. resultsand graph presented in table. Ⅵand fig. **1**respectively**.**

Calibration Data.

Concentration(µg/ml)	Absorbance
0.2	0.105
0.4	0.175
0.6	0.265
0.8	0.366

International Journal of Pharmaceutical Research and Applications
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0.10	0.423

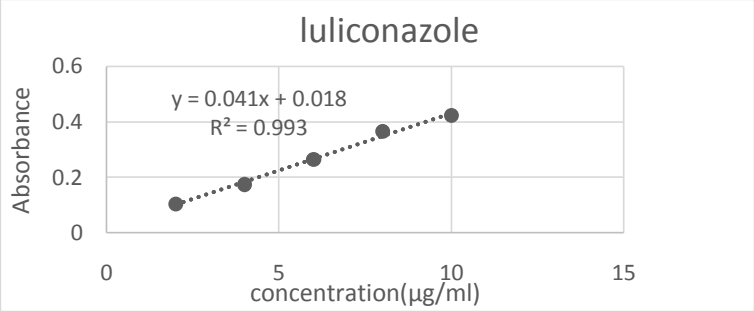

Fig. 1. Calibration Curve.

1.10. LOD and LOQ: the limit of detection (LOD)& limit of quantitation LOQ are also calculated and all result are presented in table**VII**

1.11.

Result of LOD & LOQ.

limit of detection	limit of quantitation
0.421	1.275

1.12. Precision andaccuracy:precision are performed to determine the reproducibility and the repeatability of method. Intra- day precision isperformed by standard solution of middleconcentration(0.6µg/ml) six times within the day. And inter day precision performed on two different by scanning3 concentrations (.2, .4, .6 µg/ml) six time(n=6). result ispresented in table. Accuracy of the method byspiking method at 3 level of the sample solution % recovery is calculated. Result shown in table **VIII**

result of accuracy

Parameter	%recovery	Mean	%RSD
80%	99.4028449		
	100.744767		
	101.415727	100.5211	0.008325
100%	101.539855		
	100.93599	98.44	
	92.8579271		0.040206
120%	99.9945103		
	98.0731225	98.88	
	98.8965744		0.007951

Robustness:the robustness is determined at the two different wavelength and two different scanning speed. Result are presented in table**IX**

Result of robustness and precision.

Parameter	%RSD
PRECISION	
Intra-day (n=6)	0.044
Inter-day (n=6)	0.014(.2µg/ml)

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	0.013(.4 µg/ml)
	0.010(.6 µg/ml)
ROBUSTNESS	
At 300 nm	0.0104
At 294 nm	0.0105
scanning speed (fast)	0.008
scanning speed (low)	0.0154

IX

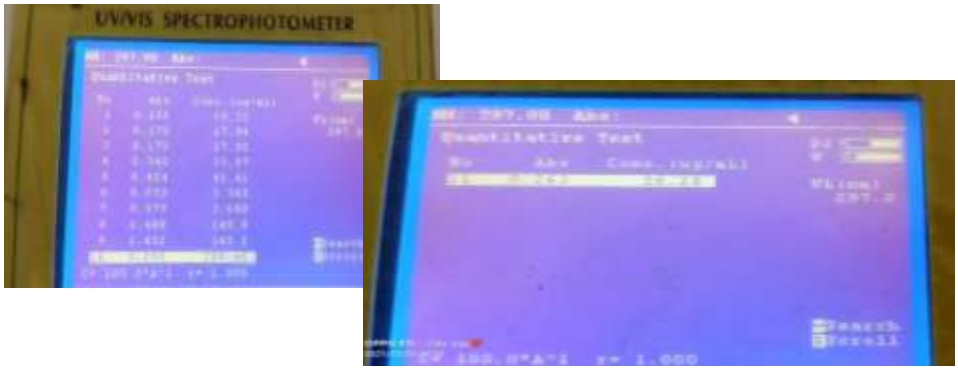

fig. a. Reading of absorbance **fig. b. Reading of absorbance**

IV. CONCLUSION:

In this study economical method for quantitative analysis of Luliconazolewas developed by the using the methanol and the process are validation are performed by determining process validation parameters such as linearity, precision, accuracy, robustness. And the simple method for Luliconazole inbulk are developed.

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