IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

SENSITIVE AND VALIDATED UV SPECTROPHOTOMETRIC METHOD DEVELOPMENT FOR ECONAZOLE NITRATE

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ABSTRACT :

A simple, precise, and cost-effective UV spectrophotometric method was developed and validated for the quantitative estimation of econazole nitrate in bulk drug. The absorption maximum (λ max) was observed at 271 nm. The method demonstrated excellent linearity within the concentration range of 5–25 µg/ml, with a regression equation of y = 0.021x + 0.0036 and correlation coefficient (R^2 = 0.999). Accuracy studies confirmed a mean recovery of 98.63%, meeting ICH acceptance criteria. Sensitivity was established with a limit of detection (LOD) of 0.957 µg/ml and a limit of quantification (LOQ) of 2.833 µg/ml. Precision studies showed % RSD consistently below 1%, indicating high repeatability and reproducibility. Ruggedness and robustness were verified under varied analytical conditions, further supporting method reliability. Collectively, these findings validate the proposed UV spectrophotometric method as accurate, precise, sensitive, and economical. The method is suitable for routine quality control of econazole nitrate in bulk powder, ensuring compliance with regulatory standards and supporting pharmaceutical quality assurance.

KEYWORDS: Econazole nitrate, UV spectrophotometric method, accuracy, precision, repeatability.

INTRODUCTION:

Econazole nitrate is an imidazole derivative antifungal agent widely used for the treatment of superficial fungal infections. It exhibits broad-spectrum activity against dermatophytes, yeasts, molds, and certain Gram-positive bacteria. Chemically, econazole nitrate is 1-[2-[(4-chlorophenyl)methoxy]-2-(2,4-dichlorophenyl)ethyl]-1H-imidazole nitrate, with an empirical formula $C_{18}H_{15}Cl_3N_2O$ and molecular weight of 444 g/mol. It is a crystalline powder ranging from white to off-white, practically insoluble in water but freely soluble in methanol and ethanol.

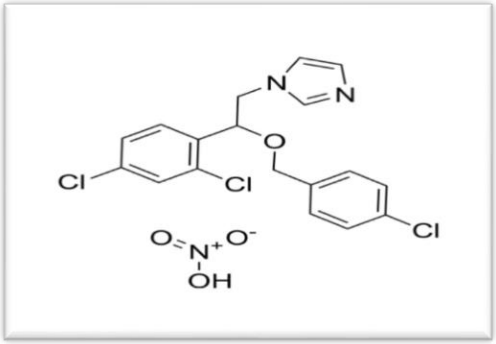


Fig. No. 1: The composition of Econazole nitrate

Its poor aqueous solubility and high lipophilicity necessitate topical formulations, which minimize systemic absorption while enhancing localized therapeutic efficacy. Pharmacologically, econazole nitrate inhibits ergosterol synthesis by interfering with 14-α-demethylase, disrupting fungal cell membranes and leading to cell death. It is indicated for tinea infections, cutaneous candidiasis, pityriasis versicolor, and vaginal candidiasis.

Analytical method development and validation are essential to ensure drug quality, safety, and efficacy. According to ICH guidelines, parameters such as accuracy, precision, linearity, specificity, robustness, LOD, and LOQ must be evaluated. UV-Visible spectrophotometry, owing to its simplicity and cost-effectiveness, is widely employed for bulk drug estimation. Econazole nitrate's aromatic rings and imidazole moiety make it suitable for UV analysis.

MATERIAL & METHOD:

Chemicals and reagents: Pure econazole nitrate (>98% purity) was obtained from Dhamtec Pharma, Navi Mumbai. Analytical-grade solvents were used.

Instruments: Shimadzu UV-1900 double beam spectrophotometer (1 nm wavelength range, 0.5 nm precision, 1 cm quartz cells), Kerro Series P3 analytical balance (0.1 mg sensitivity), and Labman sonicator were employed.

Solvent selection: Econazole nitrate was tested for solubility in distilled water, ethanol, and methanol. It was practically insoluble in water but highly soluble in ethanol and methanol. Stability studies confirmed drug stability in ethanol and methanol for 48 hours.

Standard stock solution: 10 mg econazole nitrate dissolved in methanol, sonicated, and diluted to 10 ml (1000 µg/ml).

Working solution: 1 ml of stock diluted to 10 ml (100 µg/ml). Further dilutions prepared concentrations of 5–25 µg/ml.

Wavelength selection: A 10 µg/ml solution was scanned between 200–400 nm. λmax was observed at 271 nm.

Validation parameters: Linearity, precision, accuracy, repeatability, ruggedness, LOD, and LOQ were evaluated per ICH Q2(R1).

Linearity (Calibration Curve): From the standard working solution (100 µg/ml), aliquots of 0.5–2.5 ml were transferred into 10 ml volumetric flasks. The final volume was adjusted with ethanol to prepare concentrations of 5–25 µg/ml. Solutions were scanned at 271 nm against ethanol as blank, and a calibration curve of absorbance versus concentration was plotted.

Precision (Intra-day and Inter-day): Intra-day precision was evaluated by analyzing three replicates at different concentrations on the same day. Inter-day precision was assessed by repeating the analysis over two consecutive days. Results were expressed as %RSD.

Repeatability: Six replicate absorbance measurements of a single concentration were recorded on the same day. The %RSD was calculated to confirm repeatability.

Accuracy (Recovery Studies): Accuracy was determined by recovery studies at three concentration levels (80%, 100%, and 120%). Three samples were prepared at each level (total of nine determinations). Results were expressed as mean recovery (%) and %RSD.

Limit of Detection (LOD) and Limit of Quantification (LOQ): LOD and LOQ were calculated using the following formulas:

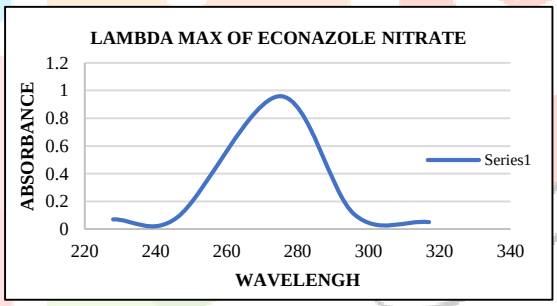
$$\boldsymbol{LOD} = \frac{3.3 \cdot \sigma}{S}$$

$$\boldsymbol{LOQ} = \frac{10 \cdot \sigma}{S}$$

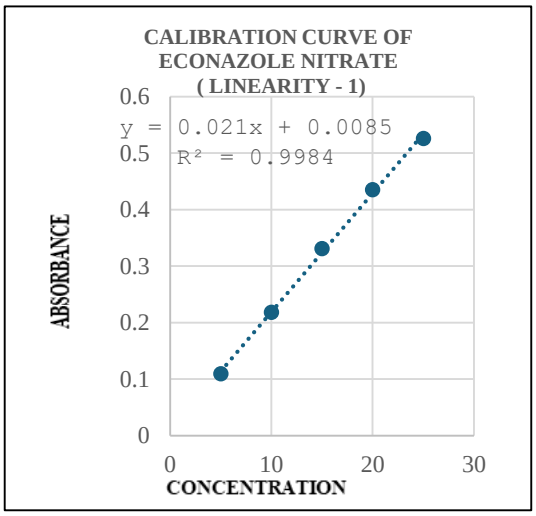
where σ is the standard deviation of the response and S is the slope of the calibration curve.

RESULT AND DISCUSSION:

Absorption maxima (λmax): The 1000 µg/ml stock solution was diluted to 100 µg/ml and scanned between 200–400 nm. The λmax was determined to be 271 nm.



Linearity (Calibration Curves): Calibration curves were prepared at concentrations of 5–25 µg/ml using three independent sets of solutions. Each curve showed excellent linearity with regression equations close to y = 0.021x + 0.0036 and correlation coefficients $R^2 \approx 0.999$. The mean calibration



curve was then plotted by averaging absorbance values from all three sets, confirming reproducibility and robustness of the method.

Figure 3: Calibration curve of econazole nitrate at 271 nm (Linearity Set 1).

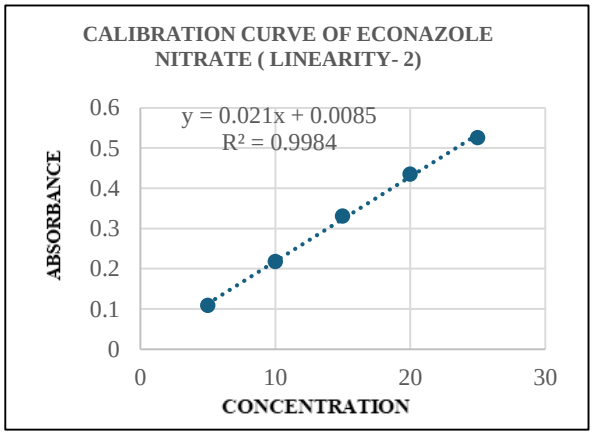


Figure 4: Calibration curve of econazole nitrate at 271 nm (Linearity Set 2).

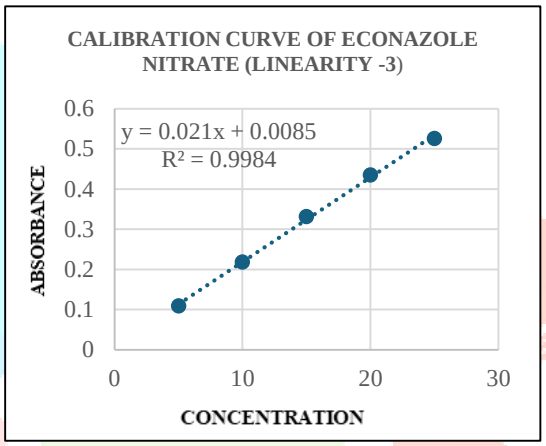


Figure 5: Calibration curve of econazole nitrate at 271 nm (Linearity Set 3)

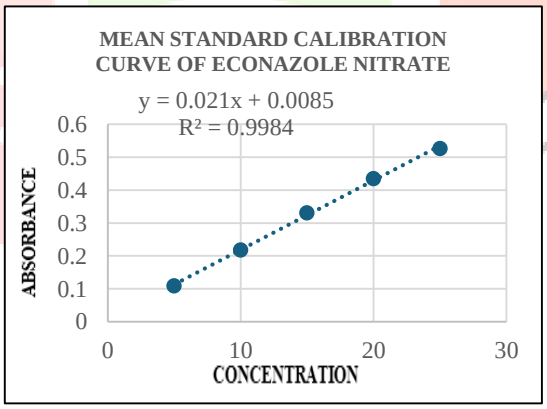


Figure 6: Mean calibration curve of econazole nitrate at 271 nm

Precision: Intra-day and inter-day precision studies confirmed %RSD <1%, indicating high reproducibility.

Table No. 1: Results for Intra-day & Inter day precision of Econazole nitrate

Concentration	Intra day Precision			Inter day Precision		
	Mean ± SD	% Amount found	% RSD	Mean ± SD	% Amount Found	% RSD
10	0.342±0.0018	99.45	0.52	0.346±0.0015	100.62	0.43
15	0.515±0.0022	100.18	0.42	0.519±0.0019	101.02	0.36
20	0.688±0.0020	99.84	0.29	0.693±0.0023	100.57	0.33
Mean % RSD			**0.41**			**0.37**

Accuracy: Recovery studies at 80%, 100%, and 120% levels yielded mean recovery of 98.63%, with %RSD values between 1.07–1.31%.

Table No. 2: Accuracy data of Econazole nitrate

Drug taken	Amount added	Absorbance maxima	Amount found	% Amount found	SD	% RSD
80%						
10	8		17.72	98.11	0.18	1.20 %
10	8		17.84	98.44	0.22	1.23 %
100%						
10	10		19.68	98.40	0.21	1.07 %
10	10		19.74	98.70	0.26	1.31 %
120%						
10	12		21.56	98.00	0.25	1.16 %
10	12		21.63	98.32	0.28	1.29 %

Repeatability: Six replicate measurements at 20 µg/ml showed %RSD = 0.26%, confirming method repeatability.

Table No. 3: Repeatability data of Econazole nitrate

Serial No.	Conc.	Abs		Amount found	SD	%RSD
1	20	0.506		19.96	0.00130	0.26 %
2	20	0.508		20.04		
3	20	0.507		20.00		
4	20	0.509		20.08		
5	20	0.506		19.96		

Ruggedness: Results obtained by different analysts and instruments remained consistent (%RSD <1%).

Table No. 4: Ruggedness studies of Econazole nitrate

Sr. no.	Name	Analyst 1	Analyst 2
		Abs	Abs
1)	Sample 1	0.4008	19.98
2)	Sample 2	0.4013	19.96
3)	Sample 3	0.4010	19.97
4)	Sample 4	0.4016	20.01
5)	Sample 5	0.4009	19.95
6)	Sample 6	0.4012	19.99
Average		19.93	19.98
SD		0.16	0.18
%RSD		0.80%	0.90%

LOD and LOQ:

According to value of the standard deviation and slope, limit of detection and limit of quantification where calculated.
LOD = 0.957 µg/ml; LOQ = 2.833 µg/ml

An overview of the validation parameters:

Table No. 5: An overview of the validation parameters:

Parameter	Your Result	ICH Acceptance Criteria	Compliance
Absorption maxima	271 nm	Characteristic λ max required	✓ Met
Linearity range	5–25 µg/ml	$R^2 \geq 0.99$	✓ Met
Regression equation	y = 0.021x + 0.0036	Consistent linear equation	✓ Met
Correlation coefficient	$R^2 = 0.999$	≥ 0.99	✓ Met
Accuracy (Recovery)	98.11–98.70%	98–102%	✓ Met
Precision (Intra-day)	0.41% RSD	≤ 2% RSD	✓ Met
Precision (Inter-day)	0.37% RSD	≤ 2% RSD	✓ Met
Repeatability	0.26% RSD	≤ 2% RSD	✓ Met
Ruggedness	0.80–0.90% RSD	≤ 2% RSD	✓ Met
LOD	0.957 µg/ml	Low, method-dependent	✓ Acceptable
LOQ	2.833 µg/ml	Low, method-dependent	✓ Acceptable

CONCLUSION:

The developed UV spectrophotometric method provides a reliable, accurate, and economical approach for the estimation of econazole nitrate in bulk drug. With excellent linearity ($R^2 = 0.999$), high recovery (~98.6 %), low LOD and LOQ values, and % RSD consistently below 1 %, the method fulfills ICH validation parameters for accuracy, precision, sensitivity, and robustness. Its simplicity and reproducibility make it highly suitable for routine pharmaceutical quality control, ensuring effective monitoring of econazole nitrate in bulk formulations.

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