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NEW VISIBLE SPECTROPHOTOMETRIC METHOD DEVELOPMENT AND VALIDATION OF KETOCONAZOLE IN PURE AND SEMISOLID DOSAGE FORM

Saili Madur*[1], Vinod Matole[1], Mallinath Kalshetti[1], Smeeta Patil[1], Aishwarya Sakhare[1]

[1*]Department of Pharmaceutical Quality Assurance, D.S.T.S Mandal's College of Pharmacy, Solapur-413004, Maharashtra, India.

ABSTRACT

Objective: A new, simple, sensitive, precise, reproducible UV visible spectrophotometric method was developed for the determination of Ketoconazole in semisolid dosage forms with chloranil. **Method:** The method is based on the formation of violet colored complex. The UV spectrum of ketoconazole in methanol and DMSO showed maximum wavelength at 481nm. Beer's law is valid in the concentration range of 5-30µg/ml. this method was validated for linearity, accuracy, precision, assay, ruggedness and robustness. **Results:** The method has demonstrated excellent linearity over the range of 5-30µg/ml with the regression equation y = 0.0232x - 0.0015, and regression coefficient i.e. r^2 = 0.9991 moreover, the method was found to be highly sensitive with LOD (2.971685µg/ml) and LOQ (0.891506µg/ml). **Conclusion:** Based on the results the proposed method can be successfully applied for the assay of Ketoconazole in various semisolid dosage forms.

KEYWORDS

Ketoconazole, UV visible spectrophotometer, Chloranil, Methanol, DMSO, Method development and Validation.

Author for Correspondence:

Saili Madur,

Department of Pharmaceutical Quality Assurance,

D.S.T.S. Mandal's College of Pharmacy,

Solapur-413004, Maharashtra, India.

Email: sailimadur253@gmail.com

INTRODUCTON

UV visible Spectrophotometer is one of the most widely used method for the development and validation of drug in bulk and pharmaceutical formulation.

Ketoconazole is an antifungal agent which contains Imidazole ring. It is used to prevent fungal infection like blasto mycosis, candidiasis, coccidioido mycosis, chromo mycosis. In Europe, it is also used in the treatment of endogenous Cushing's syndrome. It is available in market in the form of Tablet, gel, cream and injection[1].

Ketoconazole is a Lipophilic. Its nature is white crystalline powder. Solubility of ketoconazole in Dichloromethane, Ethanol, Methanol, DMF and DMSO and Practically insoluble in water. Chemical formula of Ketoconazole is $C_{26}H_{28}C_{l2}N_4O_4$ and Molecular weight is 531.431. IUPAC Name of Ketoconazole is 1-[4-(4-{[2-(2, 4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1, 3dioxolan-4yl] methoxy} phenyl) piperazin-1-yl] etan-1-one[2-4].

MATERIAL AND METHODS

Instruments

UV visible Spectrophotometry (Systronic 2201) with a 1cm quartz cuvette was used for measurement of absorbance, Weighing Balance (Shimadzu AY220), Sonicator (Oscar Ultrasonicator microclean-103).

Apparatus

Volumetric flask, Pipette, Rubber bulb etc.

Chemicals and Reagents

Ketoconazole, Methanol, DMSO and Chloranil were taken from analytical grade basis.

Experimental

Preparation of Chloranil

Chloranil 0.2% was dissolved in least amount of methanol and make up the volume upto 10ml by using DMSO.

Method Development

Preparation of Standard Stock Solution

Standard Ketoconazole solution was prepared by dissolving 10mg of drug in methanol and make up the volume upto 10ml by using DMSO. And vortex tit for 2 min at 4500rpm. And sonicate it for 10min.

Determination of Absorption maxima

From Stock solution 50µg/ml solution was prepared and scanned in the range of 200-800nm for the analysis of absorption maxima. The obtained result gives the maximum wavelength.

Procedure for determination of Calibration curve

From stock Solution (5, 10, 15, 20, 25, 30) µg/ml solutions were prepared by diluting aliquots of (0.05, 0.1, 0.15, 0.2, 0.25, 0.3) ml in methanol and make up the volume upto 10ml using DMSO.

Assay of Ketoconazole

Weigh accurately 10mg equivalent weight of ketoconazole cream and was dissolved in methanol and make up the volume upto 10ml by using DMSO. Vortex it for 2min for mixing the solution and sonicate for 10min. And then filter from formed solution aliquots were pipetted out for the range of 5-30µg/ml. and each flask add 0.5ml of Chloranil and make up the volume upto 10ml by using DMSO. The obtained result shows the parameters was validated.

RESULTS AND DISCUSSION

The absorption spectral analysis shows maximum wavelength at 481nm.

Method Validation

By using ICH guidelines, the following Parameters were validated[5].

Linearity and range

The concentration range of 5-30µg/ml at 481nm, the analytical parameter linearity was found to be linear and proportional in relationship. The regression coefficient was found to be 0.9991. The analytical parameter range is the difference between upper and lower concentration limit. The range was found to be 5-30µg/ml.

Assay

The absorbance of three dilutions of 15µg/ml of KZ cream was determined and % purity was calculated. The results are as shown in the Table.

Accuracy

The parameter accuracy is the extent to which the experimental results deviates from the expected results and it is a measure of the trueness of the analytical method. Accuracy may be reported as in Table No.3.

Precision

Intraday and Interday precision were performed by using concentration 15µg/ml. The %RSD was found within limit i.e. NMT 2%. Hence the parameter was valid.

Robustness

The deliberate change in wavelength i.e. 481nm and 487nm and concentration of 7µg/ml in the same environmental condition gave the reliable results.

Robustness

The change in analyst and laboratories with same concentration of 10µg/ml gave reproducible results. Hence the parameter was found to be validated.0

Limit of Detection (LOD) and Limit of Quantitation (LOQ)

The sensitivity of developed method was determined in terms of LOD and LOQ and it was calculated using standard deviation method.

Table No.1: Results of Linearity

S.No	Concentration (µg/ml)	Absorbance
1	5	0.105
2	10	0.239
3	15	0.349
4	20	0.469
5	25	0.578
6	30	0.691

Table No.2: Assay of Ketoconazole

S.No	Formulation	Labeled Amount	Amount obtained	% recovery
1	KZ cream	2%	1.97%	98.2%

Table No.3: Accuracy of Ketoconazole

S.No	Name of Drug	Recovery Level	Concentration	Amount Recovered	% recovery with SD
1		50	10µg/ml	10.03	100.03±0.7
2	Ketoconazole	100	20 µg/ml	19.04	99.04±0.6
3		150	30 µg/ml	30.05	100.5±0.5

Table No.4: Result for precision (Intra-day)

S.No	Concentration (µg/ml)	Absorbance
1	15	0.349
2	15	0.348
3	15	0.349
4	15	0.347
5	15	0.345
6	15	0.346
7	SD	0.001633
8	%RSD	0.470152

Table No.5: Result for precision (Inter day)

S.No	Concentration (µg/ml)	Absorbance (Day1)	Absorbance (Day2)
1	5	0.349	0.347
2	10	0.348	0.345
3	15	0.349	0.347
4	20	0.347	0.348
5	25	0.345	0.347
6	30	0.346	0.349
7	SD	0.001633	0.001329
8	%RSD	0.470152	0.382859

Table No.6: Result for Robustness

Wavelength	481nm	487nm
Concentration	7µg/ml	7µg/ml
Absorbance	0.196	0.210
	0.195	0.206
	0.200	0.199
	0.197	0.195
	0.196	0.199
	0.195	0.197

Table No.7: Result of Ruggedness

S.No	Concentration	Analyst 1	Analyst 2
1	10µg/ml	0.239	0.237
		0.238	0.234
		0.239	0.235
		0.237	0.239
		0.238	0.238
		0.239	0.300

Table No.8: LOD and LOQ

LOQ	2.971685
LOD	0.891506

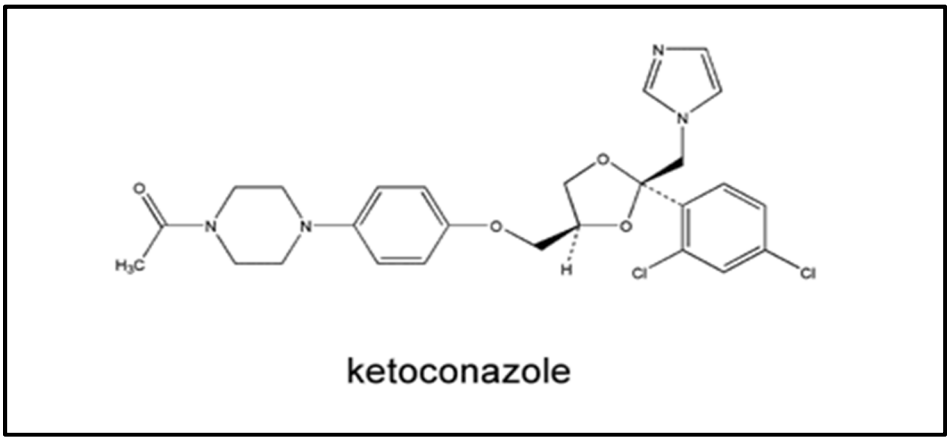

Figure No.1: Structure of Ketoconazole

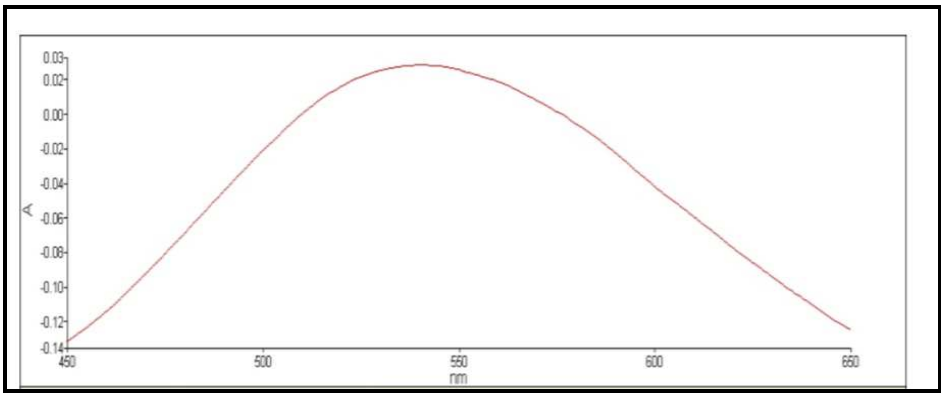

Figure No.2: UV visible Spectra of Ketoconazole

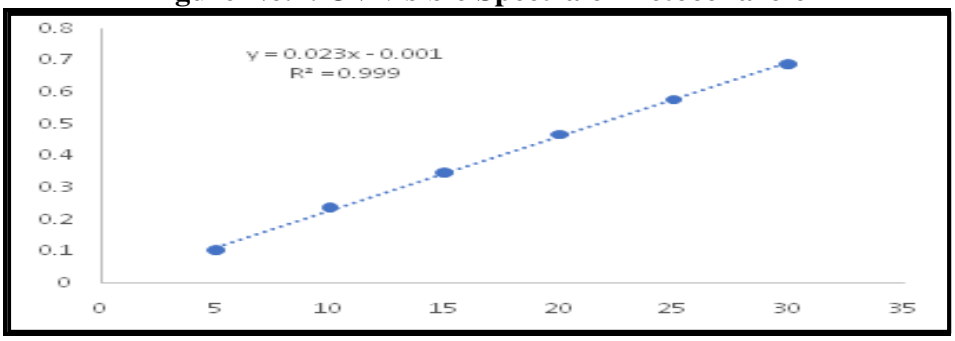

Figure No.3: Calibration curve of Ketoconazole

CONCLUSION

An analytical UV spectrophotometric method was developed and validated thoroughly for quantitative estimation of ketoconazole in API and semisolid dosage form. The above method was found to be simple, accurate, precise, reproducible and rugged.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

BIBILIOGRAPHY

1. Verma V, Kumar S. Ketoconazole HPLC method development and validation: A novel approach, *Int. Research J of Pharmacy,* 8(8), 2017, 74-81.
2. Popovska O, Rafajlovska V. A Review: Current analytical methods for determination of ketoconazole in pharmaceutical and biological samples, *IJPIJ of Analytical Chemistry,* 3(13), 2013, 1-14.
3. https://www.drugbank.ca/indications/DBCOND0060801.
4. Kavrakovski Z, Ratajkowski V. Development and validation of UV spectroscopic method for determination of ketoconazole in pharmaceuticals, *Int J Pharmacy,* 4(4), 2014, 95-101.
5. ICH, Q2 (R1) Validation of analytical procedures: text and methodology, *International Conference of Harmonization,* 1996, 111.

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