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A Sensitive HPLC Method of determination of 2-Methyl 5-Nitroimidazole & Reaction mass of intermediates of Ornidazole in Ornidazole bulk manufacturing.

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Abstract: 2-Methyl 5-Nitro Imidazole [2MNI] is the starting raw material of Ornidazole in the mfg. method described here in. Ornidazole is majorly used as Antiprotozoal as is & with combination of Ofloxacin. The present study describes a new rapid, easy Isocratic reversed phase HPLC method for the separation and estimation of intermediate as 2-Methyl 5-Nitro Imidazole and Ornidazole. The primary purpose of this study is to compile HPLC data on the determination of these products, even though they belong to one group, the compilation of such HPLC data being useful as reference guide. It was also carried out to study the feasibility of determination of any individual / combination of three intermediate using the four as the internal standards.

Key Words: Isocratic, HPLC, Determination, 2-Methyl 5-Nitro Imidazole [2MNI], Ornidazole

Introduction:

2-Methyl 5-Nitro Imidazole [2MNI] is the starting raw material of Ornidazole in the mfg. method described here in. Ornidazole is majorly used as Antiprotozoal as is & with combination of Ofloxacin (Antibiotic).[1]

Several methods are available for the estimation of the individual intermediates 2-Methyl 5-Nitro Imidazole [2MNI] in Bulk Drug and formulations using spectrometric, HPLC method etc.[2,3] The analytical chemistry of Ornidazole also has been extensively studied references on individual / combination to drug among the three is numerous. Only some of them are cited here.[4] The present study describes a new rapid, easy Isocratic reversed phase HPLC method for the separation and estimation of intermediate as 2-Methyl 5-Nitro Imidazole [2MNI] and Ornidazole. The primary purpose of this study is to compile HPLC data on the determination of these products, even though they belong to one group. The compilation of such HPLC data being useful as reference guide. It was also carried out to study the feasibility of determination of any individual / combination of three intermediate using the four as the internal standards.

The mobile phase used was Methanol [200 ml] and Water [800 ml] with pH adjusted to 7.0 the separation were carried out using fine pack silica C_{18} column [3.9 mm x 300 mm) 0.5 µ. The minimum quantifiable concentrations of all the drugs have been determined as well as the linearity range. The calculation revealed that any one of the drugs could be used as an internal standard for the determination of the drugs. Calculations pertaining to Ornidazole as internal standard have been cited in the paper, together with a detailed statistical analysis of the data.

Experimental:

Apparatus

The apparatus used was a Perkin Elmer and UV- Detector 785 A UV/VIS Detector set at 310 nm. The integration was done on a PC based Delta 5.0 software. The column comprised fine pack silica. C_{18} [3.9 mm X 300 mm] 05 µ.

Reagents–

Water and Methanol were HPLC grade, from S.D. Fine Chem. & E. Merck respectively.

Drug standard

All the drug standards were obtained from M/s. Aarti Drugs Ltd., Tarapur with certified copies of analysis. The stock solutions were prepared by dissolving 100 mg of each drug in 100 ml of mobile phase. Another stock

solution was prepared mixing the stock solution of the drug. The stock solutions were serially diluted in ten fold dilutions to the required concentration.

Mobile phase

To prepare 1 litre of mobile phase, place 800 ml Water and 200 ml Methanol into a suitable container. Mix the mobile phase thoroughly, and filter and degas under vacuum.

Assay procedure

The chromatographic conditions are listed below –

Chromatograph - Perkin Elmer System
Mobile phase – Methanol: Water (20: 80 v/v)
Column - Lechrosphere 3.9 mm x 300 mm i.e. - Stainless steel column containing C-18, 5µ ODS packing.
Detector - 785 A UV / VIS Detector
Integrator – Delta 5.0
Flow Rate – 1.0 ml/min.
Injection Volume – 20 µl
Temperature – Ambient

Retention time –

2-Methyl 5-Nitro Imidazole [2MNI] = 3.86 Min.
Ornidazole = 15.0 Min.
Run time = 30 min.

Said method is studied for its ruggedness, reproducibility and Linearity studies.

Lowest Limit of detection of all the impurities are also studied.

Recovery study shows-

Almost 98 % recovery of all the impurities along with the product (Ornidazole)

Ruggedness of the method is also shown in Table –I. & lowest limit of detection is also indicated in Table –II

Table – I: Results of Analysis of Synthetic Mixtures of 2-Methyl 5-Nitro Imidazole [2MNI] and Ornidazole.

Average of Triplicate Determinations.

Mixture No.	Ornidazole			2-Methyl 5-Nitro Imidazole		
	Taken	Found	Recovery %	Taken	Found	Recovery %
1	0.39	0.38	100.39	0.0019	0.0018	102.78
2	0.39	0.38	100.20	0.0019	0.0018	102.00
3	0.39	0.38	100.03	0.0019	0.0019	98.72
4	0.40	0.40	99.30	0.0020	0.0020	98.98
5	0.40	0.40	99.05	0.0020	0.0020	98.78
6	0.40	0.40	98.87	0.0020	0.0020	98.58
7	0.39	0.39	99.71	0.0019	0.0018	102.93
8	0.39	0.39	99.85	0.0019	0.0019	99.02
9	0.39	0.39	99.87	0.0019	0.0018	102.86

Table – II: Area Counts of Replicate Runs in Standard Mixture.

Injection No.	2-Methyl 5-Nitro Imidazole	Ornidazole
1	101.6 93	14245.9
2	103.416	14348.27
3	102.712	14457.32
4	102.569	14345.85
5	103.256	14309.63
Average	102.7292	14341.39
C.V. [%]	0.6618	0.5359

Conclusion:

External Std. Method has developed a rapid easy & accurate HPLC method for determination of all the probable impurity as 2-Methyl 5-Nitro Imidazole [2MNI].
Calculations have revealed the validity of using any one of the impurities for the estimations of other impurities.

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