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New analytical method for the quantitative analysis of ornidazole in bulk as well as various dosage forms by hydrotropic solubilisation technique

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ABSTRACT

A thorough literature survey of the various analytical methods for the quantitative estimation of Ornidazole in both bulk drug and dosage forms has revealed that very few analytical methods are available utilizing the hydrotropic solubilization technique to date. The present research paper is a description of a new analytical method developed using the principle of Hydrotropy employing very easily available chemical namely 1M Sodium benzoate solution. The method has been validated as per ICH guidelines and found to conform to ICH guidelines. In the present investigation the use of organic solvent has been avoided due to their high cost, volatility and toxicity , making the method environmental friendly. The findings revealed that the method is new, simple, safe, environmental friendly, accurate, precise, reproducible and cost-effective. It can be successfully employed as a routine analytical procedure for the analysis of Ornidazole tablets. Hence the authors suggest that this analytical method can be adopted in the Pharmaceutical industry for the analysis of Ornidazole in bulk and various dosage forms. . Ornidazole shows its maximum absorbance at 304 nm and Beer's law was obeyed in concentration range of 2-5 µg/ml in presence of 1M Sodium benzoate and Molar absorptivity was computed as 0.0065934×10^3 $mole^{-1}cm^{-1}$. Sandell's sensitivity was established as 0.0167 $\mu g/cm^2$/0.001 abs.unit. Optimum photometric range was established from the Ringbom's plot. The statistical analytical parameters namely Standard deviation and Correlation coefficient were computed and found to be 1.581, 0.996.

Keywords: Spectrophotometry, Hydrotropy, Ornidazole, Sodium benzoate.

INTRODUCTION

Ornidazole chemically is 1-(3-chloro-2-hydroxypropyl)-2-methyl-5-nitroimidazole. It has a molecular formula of $C_7H_{10}ClN_3O_3$ and a molecular weight of 219.625 g/mol [1]. Ornidazole is a derivative of 5-nitro imidazole used as an anti-infective agent [2]. Ornidazole is converted into an active form by reduction of its nitro group to amine that binds to microbial DNA and prevents nucleic

acid formation, belonging to the class of bacteriostatic [3]. Ornidazole is used for the treatment of bacterial vaginosis, trichomoniasis, genitourinary infections in women and men, amoebiasis, giardiasis. It is also used in infections against anaerobic bacteria and in the treatment of prophylaxis during surgical interventions, particularly those involving the colon, and in gynaecological operations [3]. Ornidazole has been successfully employed in combination with other drugs for peptic ulcers, few types of gastritis, stomach cancers, rheumatoid arthritis [4] and in the prophylaxis of Crohn's disease [5].

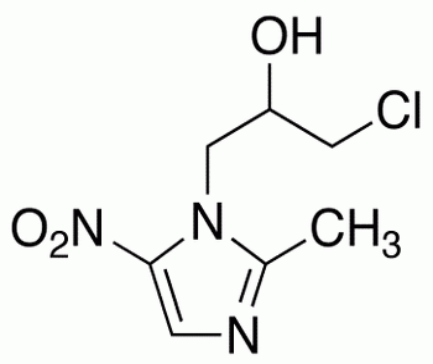

Figure-1: Molecular structure of Ornidazole

Compounds that cause increase in aqueous solubility are sometimes called hydrotropes. Concentrated aqueous hydrotropic solutions of urea, sodium benzoate, nicotinamide, sodium salicylate, sodium acetate and sodium citrate have been observed to enhance the aqueous solubility of many poorly water-soluble drugs [1-21]. The primary objective of the present investigation was to employ a hydrotropic solution to extract the drug from the fine powder of Ornidazole tablets, precluding the use of costlier organic solvents for spectrophotometric analysis. Costlier organic solvents are more often employed to solubilize the poorly water-soluble drugs for spectrophotometric analysis. Volatility and pollution are drawbacks of such solvents. Various techniques are employed to enhance the aqueous solubility of poorly water-soluble drugs. Hydrotropic solubilization is one of them. In the present investigation, hydrotropic solubilizing agent, 1M Sodium benzoate was employed to solubilize Ornidazole from the fine powder of its tablets to carryout spectrophotometric analysis. Ornidazole showed maximum absorbance at 304 nm and Beer's law was obeyed in the concentration range of 2-5µg/ml in presence of Sodium benzoate.

MATERIALS AND METHODS

Table 1: List of standard and sample details

S.NO	NAME	SUPPLIER
1	Ornidazole	Sura labs

Table 2: List of Equipment/instruments

S.NO	NAME OF INSTRUMENT	MODEL	MAKE
1	Precision balance	CA123	Contech
2	UV-Spectrophotometer	1601	Shimadzu
3	Sonicator	UCB 70	Life care

Table 3: List of Chemicals and Regents

S.NO	Chemicals/Reagents	SUPPLIER
1	Sodium benzoate	Fishers inorganics and aromatic Ltd.
2	Distilled Water	Nalanda college of pharmacy

Instrumentation

Double beam UV- Spectrophotometer (Shimadzu-1601).

Selection of wavelength of Ornidazole

The standard stock solutions of Ornidazole of 50µg/ml concentrations were scanned from 200-400nm and the maximum wavelength (λ_{max}) was recorded at 304nm wavelength in UV.

PROCEDURE FOR PREPARATION OF SOLUTIONS

Preparation of 1M Sodium benzoate solution

14.4g of Sodium benzoate was weighed and transferred in to a beaker, dissolved and made up to 100ml of distilled water until clear solution was formed.

Preparation of standard stock solution of Ornidazole

Standard stock solution of Ornidazole (500µg/ml) was prepared transferring 50 mg of Ornidazole into 100ml volumetric flask separately, dissolved and made up to 100ml with 1M Sodium benzoate solution. It was then sonicated for 10 minutes. From these, further dilutions were made using 1M Sodium benzoate to produce solution of Ornidazole (50µg/ml).

Selection of analytical concentration ranges of Ornidazole

From the standard stock solution of Ornidazole (50µg/ml), appropriate aliquots of 0.2ml, 0.4ml, 0.6ml, 0.8ml, 1ml, 1.2ml, 1.4ml were pipetted out and transferred into 10ml volumetric flasks and dilutions were made with 1M Sodium benzoate to obtain working standard solutions with concentrations ranging from 0.2 to 1.4µg/ml.

Calibration curve for Ornidazole

Appropriate aliquots from standard Ornidazole stock solutions were transferred into different volumetric flasks of 10ml capacity. The volumes were adjusted to the mark to obtain concentrations of 0.2, 0.4, 0.6, 0.8, 1, 1.2 and 1.4µg/ml. Absorbance spectra of each solution against 1M Sodium benzoate as blank were measured at 304nm and the graph of concentrations against absorbances were plotted.

ANALYTICAL METHOD VALIDATION OF UV-SPECTROPHOTOMETRIC METHOD

The analytical method was validated in accordance with ICH guidelines

Accuracy

- Accuracy is the closeness of the results obatained by the method to the true value.
- Accuracy should be established across the specified range of the analytical procedure.

Table 4: accuracy result of Ornidazole

Drug Name	Spike level	Amount added(µg/ml)	Amount found(µg/ml)	% Recovery	% of mean recovery
Ornidazole	50%	1	0.94	94	
	100%	2	1.87	93.75	96.75
	150%	3	3.07	102.5	

Precision of Ornidazole

The precision of analytical method is the degree of agreement among individual test results, when the method is applied repeatedly to multiple sampling of homogenous samples. It provides an indication of random error results.

Repeatability studies of Ornidazole

Repeatability expresses the analyte variability under the same operating conditions over a short interval of time. At least six determinations at 100% test concentration should be performed. The repeatability studies were carried out by taking 2µg/ml as the test concentration and repeating it for six times.

Linearity and range of Ornidazole

The linearity of analytical method is its ability to elicit test results that are directly proportional to the concentration of analyte in the sample within the range. The range of the analytical method is the interval between the upper and lower levels that have been demonstrated to be determined within a suitable level of precision, accuracy and linearity. The method was found to be linear in the concentration range of 2-5µg/ml. The regression equation and correlation coefficient were determined.

Sandell's sensitivity

The sandell's sensitivity is the concentration of the analyte (in $\mu g/ml^{-1}$) which will give an absorbance of 0.001 in a cell of path length 1 cm and is expressed as $\mu g\ cm^{-2}$, and it was found to be 0.0167 $\mu g/cm^2$/0.001 abs. unit.

RESULTS AND DISCUSSION

Selection of wave length of Ornidazole

The standard stock solution of Ornidazole of 50µg/ml concentration was scanned from 200-400nm and the maximum wavelength was recorded at 304nm wavelength in UV.

Table 5: Selection of λ_{max} of Ornidazole

S.no	Wavelength	Absorbance
1	200	0.136
2	213	0.173
3	226	0.191
4	239	0.224
5	252	0.232
6	265	0.251
7	278	0.254
8	291	0.276
9	304	0.294
10	317	0.278
11	330	0.264
12	343	0.246
13	356	0.223
14	369	0.191
15	382	0.148
16	395	0.119

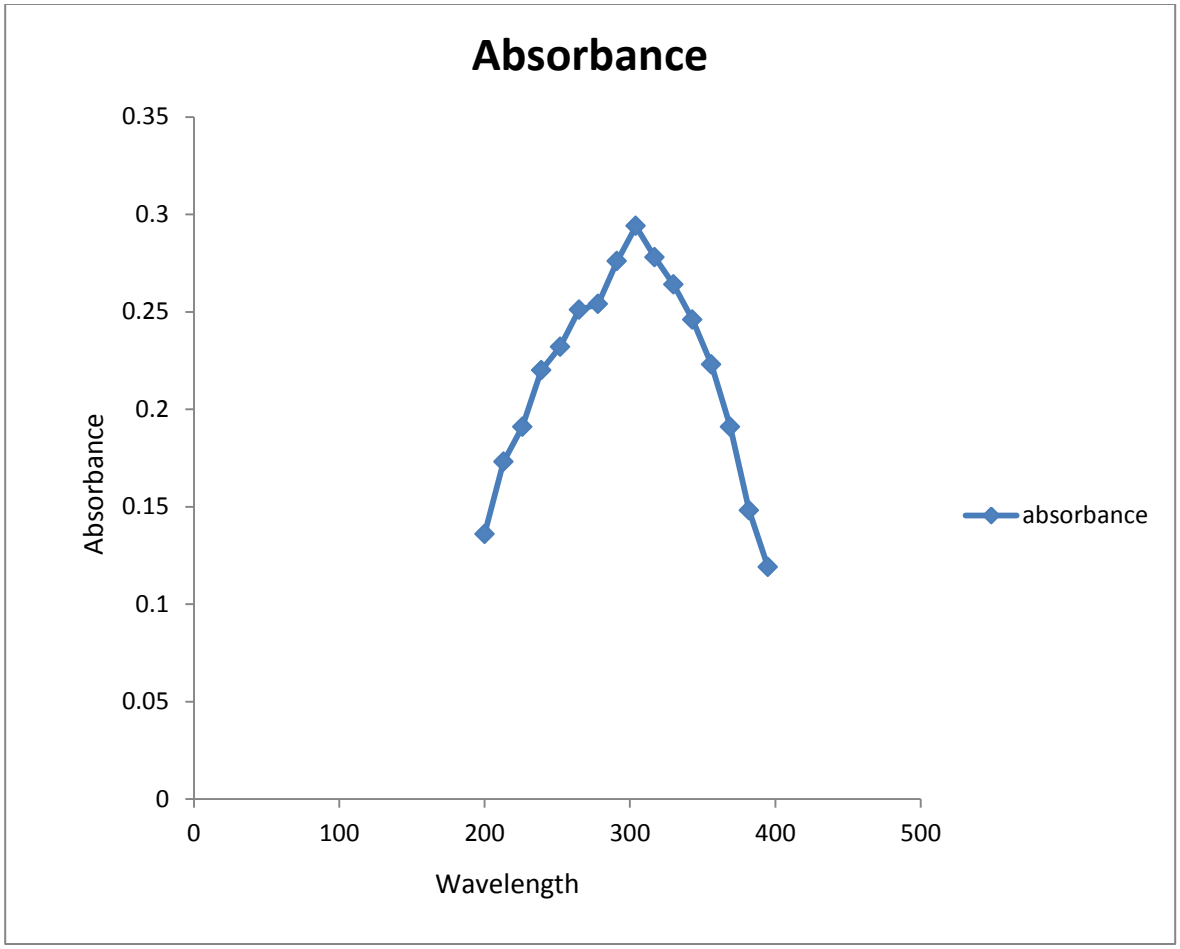

Figure-2 Selection of λ_{max} of Ornidazole

Calibration range curve (Beer's law range)

From the standard solution of Ornidazole containing 50µg/ml, different volumes containing a series of concentrations 1, 2, 3, 4, 5, 6, 7µg/ml are taken in different 10ml graduated volumetric flasks and absorbance is measured at 304nm. Beer's law was found to be obeyed in the concentration range of 2-5µg/ml. A concentration range curve and Beer's law plot are drawn taking concentration on the abscissa and absorbance on the ordinate.

Table-6 Beer's law range

S.no	Concentration (µg/ml)	absorbance
1	1	0.067
2	2	0.129
3	3	0.160
4	4	0.211
5	5	0.282
6	6	0.246
7	7	0.265

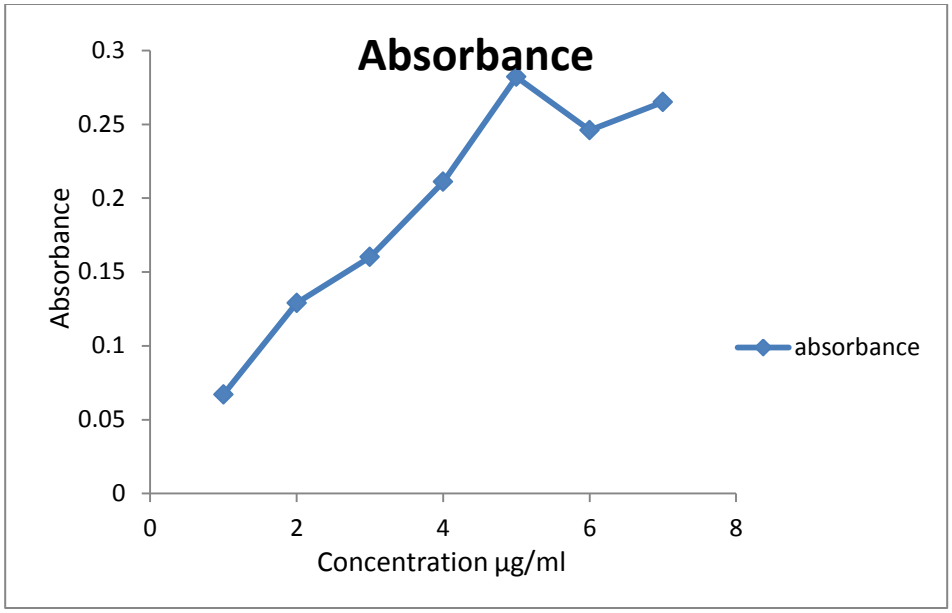

Figure-3 Calibration range curve

Calibration curve

The linearity was found in the concentration range of Ornidazole i.e. 2-5µg/ml for the developed UV spectroscopy method, by taking concentration on x-axis and absorbance on y-axis.

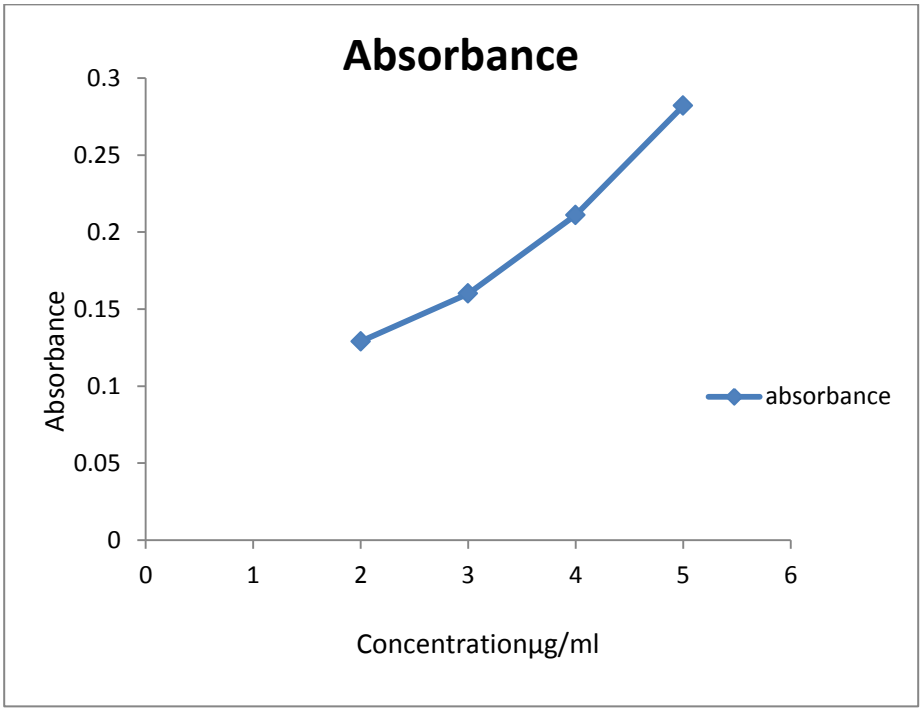

Figure-4 Calibration curve

Table 7: RESULTS OF ANALYSIS OF ORNIDAZOLE

PARAMETERS	VALUES OF ORNIDAZOLE
λmax	304 nm
Beer's law range	2-5µg/ml
Molar Extinction coefficient ($mole^{-1}cm^{-1}$)	0.0065934×10^{3}
Sandell's sensitivity ($\mu g/cm^2/0.001$abs.unit)	0.0167
Regression equation	0.0162+.0512x
Correlation coefficient(r^2)	0.996
Precision	%RSD-1.581
Accuracy (% recovery studies)	96.75%
Coefficient of variation	55.27

The results of solubility studies indicated that aqueous solubility of Ornidazole was enhanced in hydrotropic solution of 1M Sodium benzoate as compared to solubility in distilled water. So it was optimized to employ this solution in the analysis of Ornidazole in bulk and in tablet formulation. The Beer-Lambert's concentration range was found to be 2-5µg/ml for Ornidazole at the wavelength of 304 nm. The drug showed good regression value at this wave length. It was evident that there is good correlation between the amounts estimated and the label claim. Accuracy and reproducibility of the proposed method were further confirmed by the recovery studies.

CONCLUSION

It is, thus, concluded that the proposed method of analysis is novel, simple, cost-effective, environment friendly, safe, accurate and reproducible. This method can be routinely employed in the analysis of Ornidazole in tablet formulations precluding the use of organic solvent. Other poorly water-soluble drugs having λmax above 300 nm may also be tried for solubility enhancement effect using 1M Sodium benzoate solution. If the solubility is enhanced appreciably, then, this hydrotropic solution can also be employed to analyze such drugs in their solid dosage forms precluding the use of organic solvents.

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