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Development of spectrophotometric method for the determination of ornidazole in pure and pharmaceutical formulations

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ABSTRACT

Asimple, rapid and sensitive spectrophotometric method for the determination of Ornidazole, in pure and pharmaceutical formulations,has been developed and validated.

The proposed method is based on the reduction of the nitro group to amino group of the drug followed by diazotization and coupling reaction with ±-naphtol. The maximum absorbance for the obtained red colored chromogen was found at λ_{max} = 521.5 nm. The experimental conditions were optimized and Beer's law was obeyed in the concentration range of1-15 µg.ml^{-1}. Results of the analysis were validated statistically and by recovery study.

KEYWORDS

Ornidazole;
Diazotization;
Pharmaceutical preparations;
Spectrophotometric method;
Validation.

INTRODUCTION

Ornidazole is a substituted Imidazole derivative[1-3] use as anti-infective agent[1-5]. Chemically, it known as 1-(3-chloro-2-hydroxypropyl)-2-methyl-5-nitroimidazole[1,5]with molecular formula $C_7H_{10}N_3O_3Cl_1$(Figure 1).

Ornidazole is used in the treatment of anaerobic infections both pre and post operatively, bacterialvaginosis, amoebic dysentery, amoebic liver abscess, hepatic and intestinal amoebiasis, and other protozoan infection like giardiasis and trichomoniasis[1].

The antimicrobial activity of this compound is due to reduction of the nitro group to a more reactive amine group that attacks microbial DNA, inhibiting further synthesis, and leading to degradation of existing DNA[6-7].

The drug is not official in any pharmacopoeia[1,2,5,6], thus no official method is available for the estimation of Ornidazole in their dosage forms.

Literature survey shows that Ornidazole is estimated by HPLC[8], high performance thin layer chromatography[9], high and ultra-performance liquid chromatography[10], chiral liquid chromatography[11], voltametry[12], Adsorptive stripping voltametry[13], chemiluminescence[14,15], polarography[16], electrophoresis[17], potentiometry[18] andspectrophotometry[19-23] methods for its determination in dosage forms and biological fluids.

The objective of the present work is to develop and validate a simple, rapid and sensitive method to assayOrnidazoleand to determine this drug in medical Ornidazole tablets.

MATERIELS AND METHODS

Apparatus

Instrument used, for spectrum and absorbance mea-

surements, was anUV-3100 spectrophotometer with a pair of 1 cm matched quartz cells. All weighing was done on Kern ABS analytical balance. Both apparatus were calibrated and validated before starting the experimental work.

Reagents

All reagents and solvents used for study were of analytical grade. ±-naphtoland sulfamic acid were purchased from Somaprol. Distilled water was used to prepare all solutions.

Standard solutions

100 mgof Ornidazolewas accurately weighed and transferred to a 100ml beaker. 1g of zinc dust and 20ml of hydrochloric acid1M were added and well stirred. The mixture was allowed to stand for1h at room temperature and thenfiltered. The filtrate was diluted with water to 100ml in a volumetricflask. The standard solution of the reduced Ornidazole,containing 100µg.ml^{-1}, was prepared by further dilution.

A 1% α-naphtolsolution and 2% sodium hydroxide solution were kept in amber-glass volumetric flasks.A 1% sodium nitrite solution and a 2% sulfamic acid solution were prepared separately indistilled water.

Procedure

Aliquots of standard solution of reduced Ornidazole were transferred into a 20 ml calibrated flasks. 2ml of hydrochloric acid2M was added, cool inan ice bath, 2ml of 1% sodium nitrite solutionwas added andthe solutions werestirred for 2 min. 2ml of 2% sulfamicacid solution was added and the solutions were stirred for 1 min.2ml of 1% of α-naphtol solution was added. After 2min,the solutions weremade up to themark with 2% of sodium hydroxide solution.The solutions were then read at selected wavelength.

Sample preparation

10 tabletsformulation selected were crushed to obtain a fine powder. An amount equivalent to 100mg of the drug powder was reduced as mentioned above, the filtrate was made up to 100ml and analiquot of this solution was treated as described for pure sample.

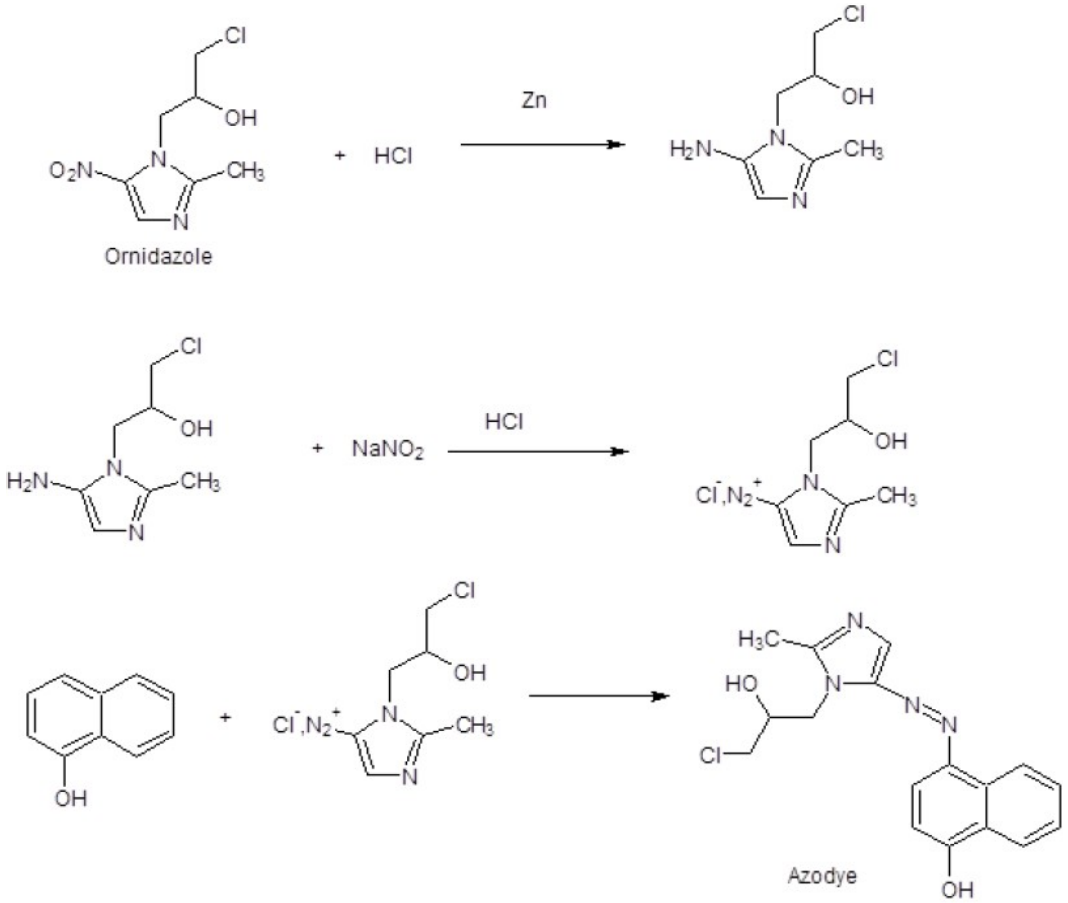

Figure 1 : Proposed reaction mechanism for the formation of red colored product

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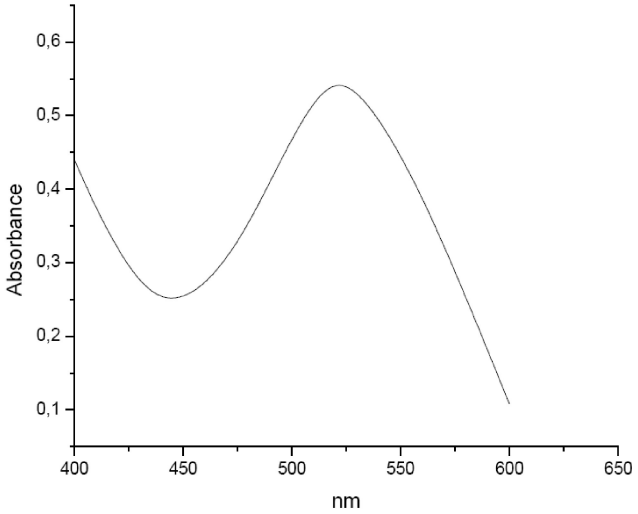

Figure 2 : Absorption spectrum of ornidazole product

RESULTS AND DISCUSSION

The spectrophotometric method for the determination of Ornidazole is based on the reduction of the nitro group to amino group, with zinc dust and hydrochloric acid, flowed by diazotization and coupling reaction with α-naphtol to give the red colored product. The stoichiometricequation derived was shown in Figure 1.

Absorption spectrum

The absorption spectra of the red colored product with λ_{max} = 521.5 nm is shown in Figure 2. The reagent blank has practically negligible absorption at this wavelength.

Optimization of reaction conditions

Factors governing the color development, the reproducibility, the sensitivity, and the conformitywith Beer's law were investigated and the formation of Azodye was optimized (TABLE 1). It was found that 2 ml of 1% sodium nitrite solution, 2 ml of 1% hydrochloric acid2M and 2 ml of 1% of á-naphtol solution were necessary to achieve maximum color intensity which corresponds to the maximum formation of Azodye.

The excess of nitrite sodium could be removed by the addition of 1ml of 2% sulfamic acidsolution. An excess of sulfamic acid has no effect on the color intensity of the formed product.

Method validation

The proposed procedure was validated by determining analytical parameters and recovery study which are given in TABLES 2-4.

TABLE 1 : Analysis of variable effects on the formation of Azodye

Serial no	$V_{NaNO21\%}$ (ml)	Absorbance	$V_{HCl\ 1M}$(ml)	Absorbance	$V_{\alpha\text{-naphtol }1\%}$ (ml)	Absorbance
1	0.5	0.487	0.5	0.522	0.5	0.482
2	1	0.511	1	0.540	1	0.458
3	1.5	0.535	1.5	0.555	1.5	0.510
4	2	0.568	2	0.563	2	0.538
5	2.5	0.540	2.5	0.534	2.5	0.506
6	3	0.470	3	0.510	3	0.488
	$V_{HCl\ 1M}$ = 2 ml $V_{\alpha\text{-naphtol }1\%}$ = 2 ml		$V_{NaNO21\%}$ = 2 ml $V_{\alpha\text{-naphtol }1\%}$ = 2 ml		$V_{NaNO21\%}$ = 2 ml $V_{HCl\ 1M}$ = 2 ml	

λ_{max} = 521.5 nm, [Ornidazole solution]= 70 ppm, $V_{Sulfamic\ acid\ 2\%}$ = 2 ml

Linearity of the method

Beer's law is obeyed; the linearity of the method was found to be over the Ornidazoleconcentration range of 1-15 μg.ml^{-1} and the linear regression value was found to be R^2 = 0.9951 (TABLE 2).

Interference study

To study the selectivity of the proposed method, some substances likely to occur in pharmaceuticals were tested for possible interferences. Theresults are given in TABLE 3.

The % recovery was found to be in the range of 99.4-100.4 %, hence there were no interferences of the excipients and additives which indicate the selectivity of the developed method.

Analytical application

To evaluate the analytical applicability of the proposed method, it was applied to the determination of amount of Ornidazole in a pharmaceutical preparation

TABLE 2 : Analytical parameters for the spectrophotometric determination of Ornidazole

Parameters\ Characteristics	Ornidazole
Color	Red
λ_{max} (nm)	521.5
stability (in days)	3
Beer's law range ($\mu g\ ml^{-1}$)	1-15
Molar absorptivity ($L\ mol^{-1}cm^{-1}$)	$1.782\ 10^3$
Regressionequation (y)[a]	
Slope (a)	0.0108
Intercept (b)	0.1785
Correlation coefficient (R^2)	0.9951
Repeatability R.S.D. (%)[b]	0.62

[a]y= ax + b where y is the absorbance and x is the concentration of Ornidazole in $\mu g\ ml^{-1}$; R.S.D. relative standard deviation; [b]average of five determination

TABLE 3 : Determination of ornidazole in presence of excipients and additives

Excipients and additives	Amount (mg)	%Recovery of Ornidazol ± RSD*
Titanedioxyde	40	100.1 ± 0.76
Talc	50	100.4 ± 0.81
Hydroxypropyl methylcellulose	50	100.14 ± 0.9
Corn starch	50	99.98 ± 0.93
Methylhydroxyethylcellulose	50	100.03 ± 0.94
Magnesium stearate	40	99.4 ± 0.84
Microcrystalline cellulose	30	99.66 ± 0.89

R.S.D. relative standard deviation; *. average of five determination

TABLE 4 : Assay of ornidazole in tiberal

Commercial Formulation analyzed	content	Label claim n mg	%Recovery of Ornidazole ± RSD*
Tiberal	Ornidazole	500/tablet	99.69 ± 0.73

R.S.D. relative standard deviation; *. average of five determination

"Tiberal". The results given in TABLE 4 indicate an excellent recovery. The %RDS less than 2 indicates that the method was accurate, precise and selective. Then, this method is suitable and can be successfully applied.

CONCLUSION

The experimental results demonstrate that the proposed spectrophotometric method is simple, economical, less time consuming, accurate, precise, reproducible and selective. Itoffers preferential advantages over most of the established procedures. Therefore, the introduced technique can be recommended for routine quality control of Ornidazolein pure form and in formulations.

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