Spectrophotometric Determination Of Metronidazole And Secnidazole In Pharmaceutical Preparations With Alpha Naphtol As A Chromogenic Reagent

ABSTRACT

A rapid and sensitive spectrophotometric method is proposed for determination of metronidazole and secnidazole. The method depends on the reduction of metronidazole and secnidazole molecule with zinc dust and hydrochloric acid followed by diazotization and coupling with α-naphtol to give red colored chromogens easily measured spectrophotometrically which has $\lambda_{\text{max}} = 483$ nm. The experimental conditions were optimized and Beer's law was obeyed over the applicable concentration ranges. Both techniques were applied successfully to a wide variety of pharmaceutical preparations.

INTRODUCTION

Metronidazole (2-methyl-5-nitroimidazole-1-ethanol) and secnidazole (1-(2-methyl-5-nitroimidazole-1-yl)propan-2-ol) are used as antiprotozoal, antiamebic and antibacterial drugs[1]. Excellent reviews have been published on the activity and pharmacokinetics of these drugs. Several methods have been reported for determination of metronidazole and secnidazole which includes potentiometric[2,3], polarographic[4,5], CPG[6], supercritical fluid chromatography[7], TLC[8], HPLC[9-12], voltammetric[13], derivative spectrophotometry[14-16], flow injection analysis[17] and spectrophotometry[18-20]. Most of the spectrophotometric methods reported suffer from the disadvantage, like narrow range of determination, requires heating or extraction, long time for the reaction to complete,
use of non-aqueous systems, stability of the coloured product formed, etc.

This paper describes sensitive and simple spectrophotometric method for the determination of metronidazole and secnidazole in either pure form or in its pharmaceuticals formulations. The method is based on the reduction of metronidazole and secnidazole molecule with zinc dust and hydrochloric acid flowed by diazotization and coupling with $\alpha$-naphtol.

The scientific novelty of the present work is that the reagents used in both the method are easily available and the chemistry of these reagents is already well established. The reactions involved with these reagents are simple, rapid and sensitive in their range of determination compared with other established methods. As Metronidazole and secnidazole are important class of imidazole compounds known for their antiamebic and antiprotozoal activity, their determination in pharmaceutical is of great importance.

**EXPERIMENTAL**

**Instrumentation**

A Perkin-Elmer 551 UV-Visible spectrophotometer with 1.0 cm matched cells was used.

**Reagents**

All chemicals used were of analytical-reagent grade. $\alpha$-Naphtol was purchased from prolabo. Sodium nitrite was purchased from prolabo. Metronidazole and secnidazole were obtained as gifts from Aventis Pharma. All other reagents and solvents were of analytical-reagent grade.

**Solutions**

Accurately weighed (100 mg) metronidazole or secnidazole was transferred to a 100 ml beaker. Add 1g of zinc dust along with 20ml 1M hydrochloric acid. Stir well and wait for 1h at room temperature, filter and the filtrate was diluted with water to 100ml in a volumetric flask. The working standard solution of the reduced metronidazole and secnidazole containing 100$\mu$g ml$^{-1}$ was prepared by further dilution. A 1% $\alpha$-naphtol solution in 1M NaOH and 10% solution of hydroxyde de sodium were kept in amber-glass volumetric flasks.

A 1% sodium nitrite solution and a 2% sulfamic acid solution were prepared separately in distilled water.

**Procedure**

Aliquots of the working standard solution of reduced metronidazole or reduced secnidazole were transferred into 10 ml calibrated flasks. 1ml of 1M HCl was added, cool in an ice bath and add 2ml of 1% NaNO$_2$, stir the solution for 2 min. Add 1ml of 2% sulfamic acid, stir the solution for 1 min and add 1 ml of 1% of $\alpha$-naphtol. After 2min made up to the mark with 10% of NaOH solution.

**Assay of pharmaceutical tablets**

Twoelve tablets were powdered and mixed thoroughly. An amount equivalent to 100 mg of the drug was reduced as mentioned in and the filtrate was made up to 100ml and an aliquot of this solution was treated as described above for pure sample in both the method.

**RESULTS AND DISCUSSION**

The spectrophotometric method for the determination of metronidazole and secnidazole is based on the reduction of the nitro to an amino group with zinc dust and hydrochloric acid flowed by diazotization and coupling with $\alpha$-naphtol to give red colored product.

**Spectral characteristics and reaction mechanism**

The absorption spectra of the red coloured product with $\lambda_{max} = 483$ nm are shown in. The reagent blank has practically negligible absorption at this wavelength. The stochiometric equation derived was shown in SCHEME 1.

**Optimization of reactions conditions**

The factors affecting color development, reproducibility, sensitivity, and conformity with Beer’s law were investigated.

For the maximum formation of azodye, a volume of 1% NaNO$_2$ solution was optimized. The results are shown in TABLE1. As can be seen, 2ml of nitrite solution was found to be the optimum vol-
Quantification

Beer’s law is obeyed over the metronidazole concentration range of 1-15 µg/ml. Similarly, for secnidazole, Beer’s law is obeyed over the concentration range of 1-15 µg/ml. The proposed procedure is validated by determining various optical parameters, which are listed in TABLE 5.

Interference

The extent of interference by common ions were determined by measuring the absorbance of a solution containing 20 µg ml⁻¹ of metronidazole or secnidazole solutions.
and various amounts of diverse species. Majority of the common ions do not interfere. An error of 2% in the absorbance readings was considered tolerable. Some of the common excipients, which often accompany the pharmaceutical preparations, do not interfere in the present method. The results are given in TABLE 6.

### Analysis of pharmaceutical preparation

Application of the proposed method to the determination of metronidazole and secnidazole drugs in its dosage forms was successfully made; the results are presented in TABLE 7. The excellent recoveries obtained indicated the absence of any interference from the excipients.

### CONCLUSION

The method is found to be simple, economical, selective and more sensitive than most of the spectrophotometric methods reported. The statistical parameters and recovery study data clearly indicate the reproducibility and accuracy of the method. Analysis of the authentic samples containing metronidazole and secnidazole showed no interference from the common excipients. Hence, this approach could be considered for the determination of metronidazole and secnidazole in the quality control laboratories.
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REFERENCES