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Novel and Rapid Estimation of Metronidazole in Tablets

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Abstract

Simple aqueous titrimetric method is developed for the determination of metronidazole in tablets. The proposed method is based on the reduction of the nitro group to amino group of the molecule with zinc and 6M HCl. The reduced molecule was diazotised with sodium nitrite at 5-10^{o}C. The reactions were carried out in aqueous medium without the use of organic solvents. This method was validated by low values of statistical parameters viz, standard deviation, related standard deviation and standard error of mean. This method is novel, accurate and economic and eco-friendly. The proposed method is recommended for quality control, routine analysis and developed for academic purpose.

Keywords: Metronidazole, Reduction and Diazotization

INTRODUCTION

Metronidazole belongs to 5-nitroimidazole group, and extensively used as antiamoebic, antiprotozoal and antibacterial drugs. The discovery of the antibacterial and antitrichomonal properties of the antibiotic azomycin led to the investigation of nitroimidazoles as antiparasitic agents [1]. In laboratory tests, metronidazole is effective against intestinal amoebiasis in rats and hepatic amoebiasis in hamsters and is also active against *Entamoeba histolytica* in vitro [2, 3]. The initial clinical tests of metronidazole indicated that it was capable of curing invasive amoebic dysentery and amoebic liver abscess [4]. Subsequent clinical tests have established metronidazole as the drug of choice in the treatment of all forms of amoebiasis in humans [5,6].

Metronidazole is officially determined by titrimetry, potentiometry and HPLC methods. Indian Pharmacopoeia [7] describes the non-aqueous titration method using perchloric acid as titrant and malachite green as indicator for the assay of metronidazole. British Pharmacopoeia [8] describes potentiometric and non-aqueous titration methods using perchloric acid as titrant. United States Pharmacopoeia [9] describes HPLC and nonaqueous titration methods for the assay of metronidazole. Several methods have been reported for the determination of

metronidazole, including spectrophotometry [10,11, 12] and polarography [13]. Most of the spectrophotometric methods found in the literature for the determination of metronidazole in the visible region involve initial reduction by treatment with Zinc powder and HCl followed by the diazotization and coupling of the resulting amine [14 – 21]. All these methods involve tedious procedures such as heating and extraction using various organic solvents which include toxicity, utilize complex reagents which are expensive and environmental hazards.

The main objective of this study was to avoid organic solvents and the estimation of metronidazole was carried out in aqueous medium without using sophisticated instruments like spectrophotometer, HPLC, etc.

MATERIALS AND METHODS

Reagents

All reagents used were of analytical grade and were obtained from M/S.BDH Laboratory Supplies, England. Metronidazole tablets were purchased from the local market. Distilled water was used for the preparation of solutions.

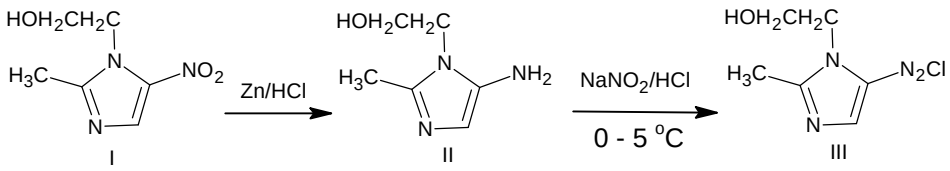
Experimental

Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.1 g of metronidazole and suspended in 30ml of 6N hydrochloric acid. To this 0.5 gm of zinc powder was added and kept aside with occasional shaking until the reaction completes. The reaction mixture was filtered to a conical flask using a Whatman filter paper No 41 to remove the insoluble matter. The residue was washed with 10 mL portions of water three times, and the solution was cooled to 5-10^{o}C. To this 0.5 gm of potassium bromide was added and the reaction mixture was titrated with 0.1.M sodium nitrite solution using starch iodide paper as external indicator. The end point can also be detected by electrometric method. Each ml of 0.1.M sodium nitrite is equivalent to 0.01712 g of $C_6H_9N_3O_3$. The amount of metronidazole present in the sample was calculated.

Five marketed products of metronidazole tablets were taken for analysis and each products was estimated five times. The values were analyzed by statistical methods using Graphpad Instat software.

RESULTS AND DISCUSSION

The aromatic nitro group present in the metronidazole (I) was reduced to amino group (II) by carrying out reduction with zinc and Hydrochloric acid. The reduced metronidazole was diazotized with sodium nitrite to give diazonium salt of metronidazole (III). The reaction is depicted in the following scheme.



The optimum conditions for the estimation are established by varying the parameter one at a time and keeping other parameters fixed and observing the effect on the assay.

To study the quantity of zinc required for reduction was done by performing the assay with 0.1/0.2/0.3/0.4/0.5/0.6/0.7 grams of zinc separately and satisfactory results were obtained with 0.5 grams of zinc powder.

The concentration of hydrochloric acid was determined by performing the assay with 30 ml of 1N/2N/3N/4N/5N/6N/7N of hydrochloric acid separately and satisfactory results were obtained with 6N Hydrochloric acid.

A study of interferences of excipients has been made during the determination of metronidazole. It was observed that starch, glucose and lactose were added to the powder of metronidazole tablet and results obtained shows that in the proposed method excipients are not interfered in the estimation.

The proposed method for the assay of metronidazole was tested with various available commercial formulations. The results are given in the Table. The analysis showed that the data are consistent with the label claim of the formulations. The method is validated statistically by low values of percent coefficient of variation, standard deviation and standard error. The reproducibility and recovery studies show that the method is precise and accurate. In addition, it is observed that there is no interference from the excipients used in the formulations. Hence, this method can be adopted for the routine quality control of metronidazole in tablet formulations.

Table: Analysis data of metronidazole tablets with statistical evaluation

Name of the Product	**Statistical Values**			
	Mean % Estimated	Standard Deviation	Related Standard Deviation	Standard Error of Mean
Neogyl 500	100.142	0.7187	0.7178	0.3214
Anazol 500	99.658	0.6313	0.6335	0.2823
Negazole 500	99.968	0.4772	0.4774	0.2134
Flagyl 250	99.95	0.1313	0.1314	0.0587
Metrogyl 250	100.204	0.7122	0.7108	0.3185

CONCLUSION

The proposed method is simple, sensitive, accurate, precise, economical and moreover, it is environmentally benign methodology since no organic solvents is required for the analysis and does not require any pretreatment of the drug and tedious extraction procedure prior to its determination. This method can compete with any other existing assay methods for the routine quality control analysis of metronidazole in pharmaceutical formulations.

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