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STABILITY INDICATING UV-SPECTROSCOPIC METHOD FOR OFLOXACIN AND TINIDAZOLE IN COMBINED DOSAGE FORM

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ABSTRACT

A simple, specific, stability indicating study by UV-Spectrophotometric method for ofloxacin and tinidazole in combined dosage form using a Shimadzu model spectrophotometer with 0.1 N Hcl at wavelength λmax at 227 nm and 312 nm for ofloxacin and tinidazole respectively. The drug was subjected to acid, neutral, alkali, oxidation, thermal and thermal degradation. While estimating the commercial formulation there was no interference of excipients and other additives. Hence this method canbe used for routine determination of ofloxacin and tinidazole in their bulk and pharmaceutical dosage forms. The proposed method for stability study shows that there was appreciable degradation found in stress condition of the drugs.

KEYWORDS: *ofloxacin , tinidazole, degradation, UV Spectroscopy etc.*

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INTRODUCTION

Ofloxacin , (+) 9-fliuoro-2,3, dihydro -3- methyl -10 –(4-methyl-1-piperaznyl)-7-oxo-7H –pyrido [1,2,3-d,e]-1,4-benzoxazine -6-carboxylic acid, is one of the new generation of fluorinated quinolone structurally related to nalidixic acid[1]. This agent is a new broad spectrum antibacterial drug active against most Gram negative, Gram positive bacteria and some anaerobes. This broad spectrum of antibacterial activity and wide spread distribution to most tissues and body fluids at relatively high concentration after oral administration have made this drug useful for the treatment of systemic infections including urinary tract, respiratory and gastro intestinal infections[2]. Tinidazole [1-(2-ethylsulfonyethyl)-2-methyl-5-nitroinidazole] is a 5 –nitroimidazole derivative, an antiparasitic drug used against protozoan infections. It is also used in the treatment of a variety of amebic and parasitic infections.

Literature survey reveals that OFL was determined by several methods including spectrophtotmetric, HPLC, extractive spectrophotometric method and chemiluminescene method [4]. Capillary electrophoresis, HPLC,spectrophotometric and

capillary electrophoresis methods have been reported for the estimation of OFL in combination with other drugs[5]. TNZ was determined by spectrophotometric, HPLC, and electrochemical study [6]. Some methods have also been reported for the determination of TNZ in combination with other drugs including spectrophotometric, capillary electrophoresis and differential pulse polarography[7]. Literature survey revealed that spectrophotometric and HPLC methods have been reported for the estimation of OFL and TNZ in pharmaceutical formulations [8-10]. The aim of this paper was to carry out the stability indicating study of ofloxacin and tinidazole in bulk and in their combination.

The API is subjected to a number of force degradation conditions which include acidic, basic and oxidative conditions. Force degradation should be one of the activities performed early in the development process to ensure that the method is discriminating between the API and degradants. Depending on the API, not every stress agent may affect degradation, but each agent has to be evaluated to determine whether degradation occurs.[11]

MATERIALS AND METHOD:

Chemicals, materials and equipments:

A SHIMADZU model PHARMASPEC-1800 UV-Vis spectrophotometer with 1.0 cm matched cells was used for the electronic spectral measurements. Ofloxacin, tinidazole and all other chemicals used were analytical reagent grade. Ofloxacin and tinidazole pure drug was generously provided by Torrent Pharmaceuticals Pvt ltd (Ahmadabad, India), as a gift sample. The commercially available tablet "oflox –TZ" (Cipla pharmaceuticals) containing 200 mg ofloxacin and 600 mg tinidazole was procured from the local market

METHOD:

Preparation of standard solution:

The standard stock solution was prepared by dissolving 10 mg of the drug in 100ml of 0.1 N Hcl to get a concentration of 100 µg/ml. This solution is further diluted to get a concentration of 5-10 µg/ml of ofloxacin and 10-60 µg/ml of tinidazole.

Preparation of sample solution:

Twenty tablets was weighed and powdered. The powder equivalent to 150 mg of tinidazole was transferred to 100ml volumetric flask and treated with 100ml of diluent. This solution was filtered through 0.45 µm membrane filter. This filtered solution was diluted with diluent to get the final concentration of ofloxacin 10 µg/ml and tinidazole 30 µg/ml.

Procedure for forced degradation:

Degradation studies were performed in tablet solution containing ofloxacin 200 mg and tinidazole 600mg.

Stress degradation by hydrolysis under acidic conditions:

For acid degradation, weighed 10 mg drug was taken and made upto10ml with 0.1N Hcl and refluxed for 5h at 60^0. The absorbance was measured in every hour by withdrawing the required amount of sample from reaction mixture and subjected for UV analysis.

Stress degradation by hydrolysis under alkaline conditions:

For alkali degradation weighed 10 mg drug was taken and made upto10ml with 0.1N NaOH and refluxed for 5h at 60^0. The absorbance was measured in every hour by withdrawing the required amount of sample from reaction mixture and subjected for UV analysis..

Stress degradation by hydrolysis under neutral conditions:

For neutral degradation weighed 10 mg drug was taken and made upto10ml with distilled water and refluxed for 5h at 60^0. The absorbance was measured in every hour by withdrawing the required amount of sample from reaction mixture and subjected for UV analysis

Oxidative degradation:

For oxidation, weighed amount of drug was made up to 10 ml with 3% H_2O_2. The solution mixture was kept in dark condition for 12 h. Each 6h interval the specified amount of sample withdrawn and the required concentration was prepared and determined the absorbance.

Photolytic degradation:

For photolytic degradation,the tablets were powdered and weighed and kept in petridish under direct sunlight for three days. After the specified interval the required amount of sample was withdrawn and the absorbance was measured.

Thermal degradation:

A specific amount of bulk drug was taken in a clean petridish and was put it in an oven at 60^0 for determining thermal degradation.

RESULTS AND DISCUSSION:

Stress Degradation Study

ICH guidelines recommend 10-20% degradation for establishing stability indicating nature of the assay method. The degradation study indicated that Ofloxacin was susceptible to alkaline, oxidative and thermal degradation more than acidic and photolytic degradations. For tinidazole degradation was obtained in basic, acidic and H2O2 condition. The summary of the degradation is given in the table 1,2

Stress condition	Time	% assay of degraded product	% assay of active substance
Acidic hydrolysis	5h	75.1	25.9
Alkaline hydrolysis	5h	6.01	93.98
Neutral hydrolysis	5h	70.57	29.43
Photolytic degradation	12h	37.01	62.98
Thermal degradation	12 h	62.4	37.6
Oxidative degradation	12h	29	71

TABLE 1: SUMMARY OF STRESS DEGRADATION RESULTS OF OFLOXACIN

Stress condition	Time	% assay of degraded product	% assay of active substance
Acidic hydrolysis	5h	40.71	50.79
Alkaline hydrolysis	5h	16.93	83.06
Neutral hydrolysis	5h	49.89	50.11
Photolytic Degradation	12h	9.44	90.55
Thermal degradation	12h	97.01	3
Oxidative degradation	12h	46.1	53.9

TABLE 2: SUMMARY OF STRESS DEGRADATION RESULTS OF TINIDAZOLE

CONCLUSION:

The method is specific while estimating the commercial formulation without interference of excipients and the other additives. The proposed method for stability study shows that there is appreciable degradation found in stress condition of ofloxacin and tinidazole. A new simple analytical method was developed to be applied for the evaluation of the stability of ofoxacin and tinidzole. In addition to demonstrate specificity, forced degradation study can be used to determine pathways and degradation product of APIs that could form during storage and facilitate formulation, development, manufacturing and packaging.

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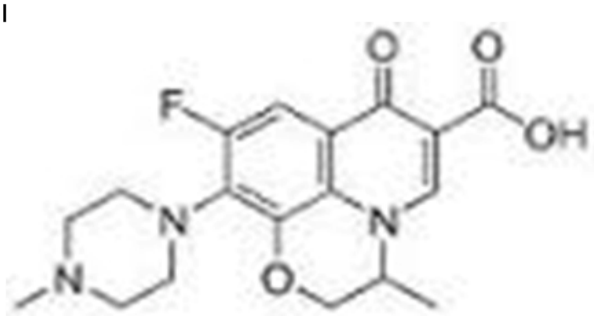

FIGURE 1: Structure of ofloxacin

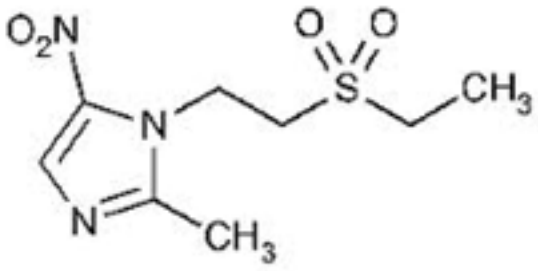

FIGURE 2: Structure of tinidazole.

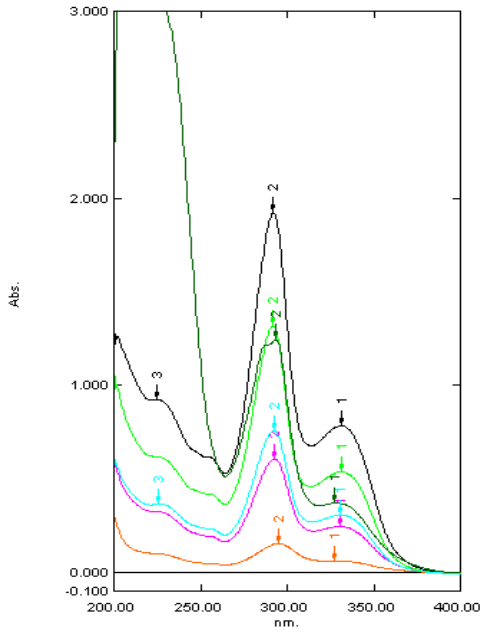

FIGURE 3 : Alkaline degradation spectrum of ofloxacin

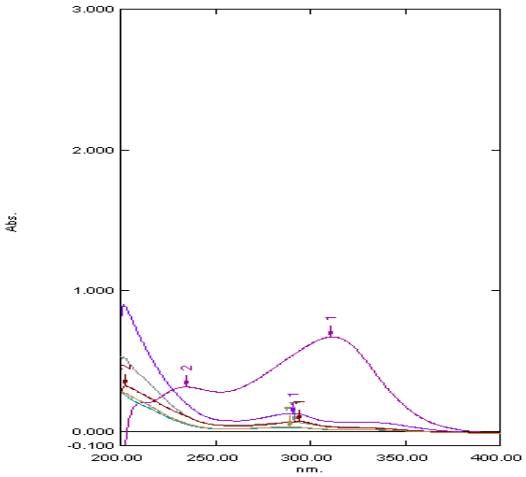

FIGURE 4 : Alkaline degradation spectrum of tinidazole.

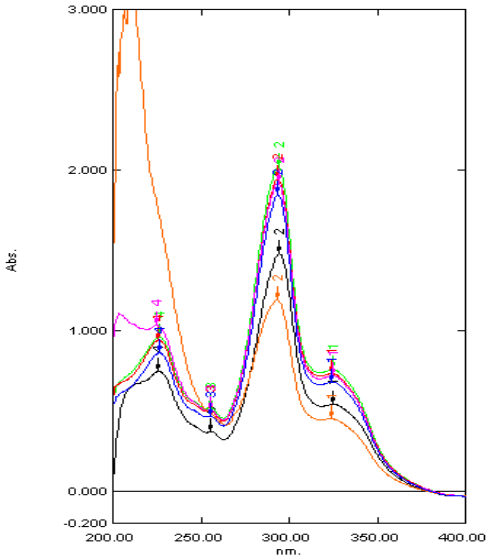

FIGURE 5 : : Acidic degradation spectrum of ofloxacin

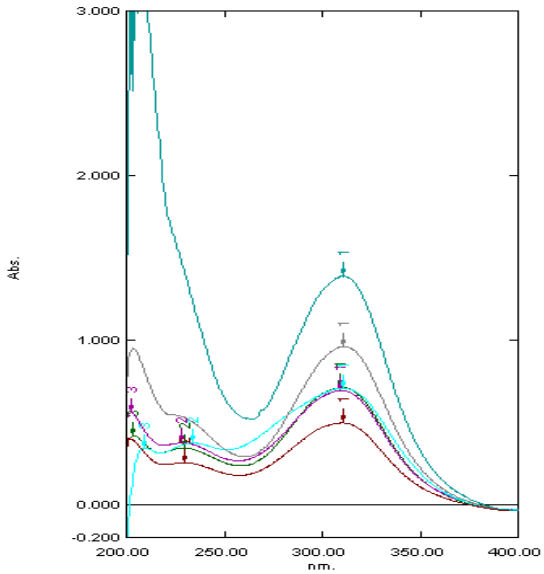

FIGURE 6: Acidic degradation spectrum of tinidazole.

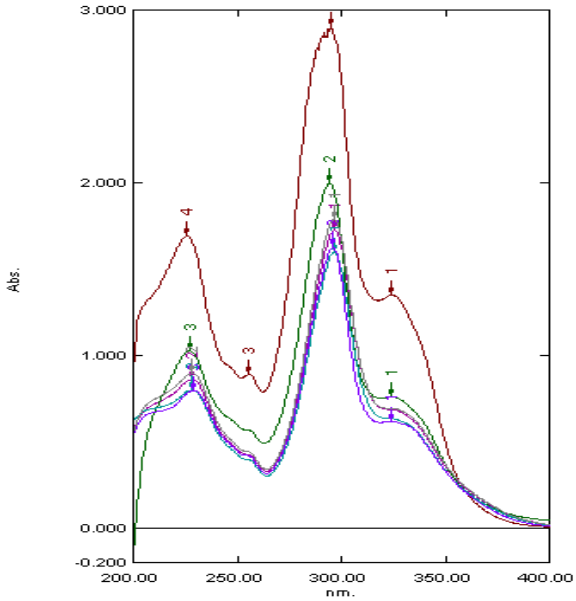

FIGURE 7 : neutral degradation spectrum of ofloxacin

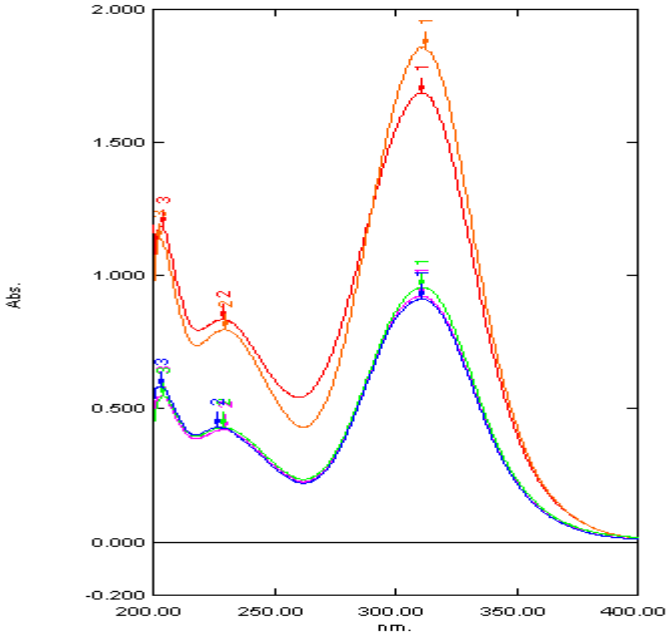

FIGURE 8: neutral degradation spectrum of tinidazole

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