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SIMULTANEOUS QUANTITATIVE DETERMINATION OF TINIDAZOLE AND DILOXANIDE FUROATE IN TABLET PREPARATIONS BY DIFFERENCE SPECTROSCOPY

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ABSTRACT

A difference spectrophotometric procedure has been developed for the simultaneous determination of Tinidazole (TD) and Diloxanide furoate (DF) in tablet preparations. The method comprised the measurement of absorbance of a solution of the tablet extract in pH 2.0 buffer solution relative to that of an equimolar solution in pH 13.0 buffer at the wavelengths of 282nm and 240nm. The presence of identical isosbestic points for pure drug samples and tablet extract solutions indicated the non-interference of excipients in the absorption at these wavelengths. The compliance of Beer's Law was obtained in the concentration range of 20-40µg/ml for TD and DF at these wavelengths.

INTRODUCTION

Difference spectrophotometry is the technique which involves the reproducible alteration of the spectral properties of the analyte in equimolar solutions and the measurement of the absorbance difference(δA) between two solutions. Its advantages for selective analysis of drugs without specific interferences have been described by some workers.[1,2] A combination of TD and DF is widely used for acute and chronic intestinal amoebiasis and hepatic amoebiasis.[3] Some methods have been reported for the individual assay of TD[4,5] and DF[6,7,8.] but there are no reports about their simultaneous determination in the presence of each other. The later is being discussed in the present research work.

EXPERIMENTAL

Standard and Sample Solutions

Appropriate aliquots of stock solutions of pure TD (1mg/ml) and DF(1mg/ml) in methanol were used to prepare two series of equimolar solutions of each drug in pH 2.0 and 13.0 buffers containing 20-40μg/ml of TD (series I) and 20-40μg/ml of DF (series II). Similarly, two more series of equimolar solutions of mixtures of

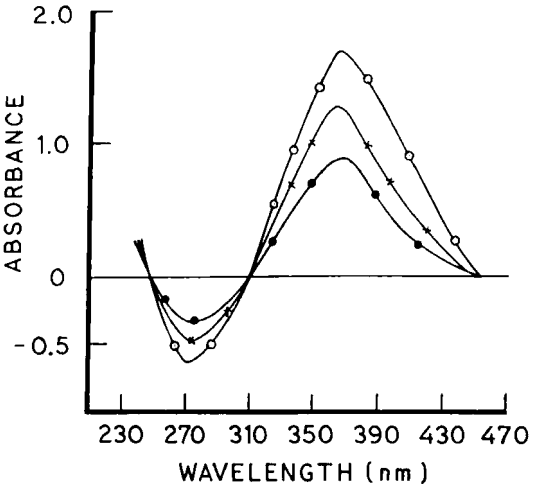

FIGURE 1.

Difference Absorption Spectra of Tinidazole in pH 2.0 versus pH 13.0 solutions
(-●-●-●-) 20µg/ml (x-x-x-x) 30µg/ml
(-○-○-○-) 40µg/ml

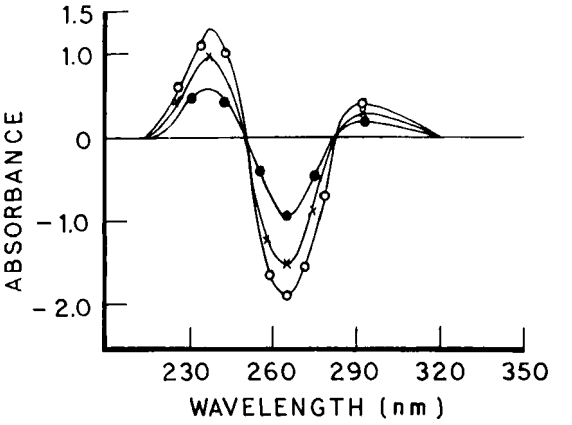

FIGURE 2.

Difference Absorption Spectra of Diloxanide furoate in pH 2.0 versus pH 13.0 Buffer Solutions
(-●-●-●-) 20µg/ml (x-x-x-x) 30µg/ml
(-○-○-○-) 40µg/ml

TABLE 1

Assay Results of Tinidazole and Diloxanide furoate in Commercial Formulations by Difference Spectroscopy.

Sample	TD		DF	
	mg/tab	%w/w stated*	mg/tab	%w/w stated*
Brand A	298.5	99.50 ± 0.4621	498.8	99.76 ± 0.5156
Brand B	297.3	99.10 ± 0.2302	498.0	96.60 ± 0.2701
Brand C	299.4	99.80 ± 0.3391	247.5	99.00 ± 0.3898

* Five replicate measurements

TD and DF, the first containing a constant concentration of 30µg/ml of DF and a varying concentration of 20-40µg/ml of TD (series III) and a second containing a constant concentration of 30µg/ml of TD and a varying concentration of 20-40µg/ml of DF (series IV) were prepared with the buffers.

Twenty tablets were accurately weighed, powdered and a weight of the powder equivalent to 50mg of TD (and 83mg or 41mg of DF) was dissolved in methanol, filtered, and appropriate volumes of the aliquots were diluted with the buffers to obtain equimolar solutions containing approximately 25µg/ml of TD and 40µg/ml of DF respectively .

The absorbance difference of the acidic and basic equimolar drug solutions were measured from 230-350nm with a Jasco 7800 uv-visible double beam spectrophotometer. The results are given in Table 2.

RESULTS AND DISCUSSION

The δA values of standard solutions of TD (25μg/ml) and DF(40μg/ml) relative to δA of tablet sample solution was used for the determination of TD and DF in the tablet preparation.The concentration of TD and DF in the tablet contents of average weight as a percentage of stated quantity of drug were calculated using well established procedure[9]. The results are given in Table 1.

The wavelengths of δA value maxima,minima and isosbestic points (a wavelength of zero δA due to equal absorptivities of the two species) of TD and DF spectra are shown in Fig 1 and 2 respectively. The wavelengths of 282nm and 240nm were chosen for the estimation of TD and DF since the δA values of their difference spectra were more optimal for accurate absorption measurement than the value at the other isosbestic points for the concentrations of TD and DF in commercial formulations as well as to provide minimum relative error in absorption measurement. The regression equations of the solutions of series

TABLE 2

Method Selectivity for the Determination of Tinidazole and Diloxanide furoate by Difference Spectroscopy

Composition of mixture µg/ml TD	DF	Mean* (δA)	95% Confidence Limit**
20	20	0.325 ± 0.0022	± 0.0012
30	20	0.484 ± 0.0022	± 0.0021
40	20	0.653 ± 0.0028	± 0.0014
20	20	0.664 ± 0.0037	± 0.0018
20	30	0.992 ± 0.0032	± 0.0015
20	40	1.322 ± 0.0038	± 0.0021

* Ten replicate measurements
** Based on student's t distribution

I,II,III and IV (mentioned under Standard Solutions) were y = 0.162x + 0.0010 (RE I), y = 0.032x + 0.0025 (RE II), y = 0.162x + 0.0025 (RE III) and y = 0.032x - 0.0017 (RE IV) with corresponding correlation coefficients of 0.9984, 0.9998, 0.9986 and 0.9998 respectively. The similarity of RE I to RE III and RE II to RE IV suggest the non-interference of the absorptivity of the drugs with each other as well as excipients at the isosbestic points.

CONCLUSION

Difference spectroscopy may be used for the analysis of such two component formulations in which the isosbestic point of one component lies at or near the maximum of the difference spectrum of the other component. The proposed method meets these requirements. The non-interference of the excipients in the determination is evidenced by the identical isosbestic points in the standard and sample solutions. The similarity of the regression equations indicate the rectilinearity of δA values at the isosbestic points and specificity of the method. The negligible intercepts and similar correlation co-efficients confirm the precision and reproducibility of the method. Hence the proposed method is found suitable for the simultaneous determination of TD and DF in tablet formulations.

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