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Short Communication

Simultaneous spectrophotometric determination of diloxanide furoate and metronidazole in dosage forms

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Introduction

Mixtures of diloxanide furoate–metronidazole are used for the treatment of non-dysenteric intestinal amoebiasis and is considered to be the drug of choice for this form of the disease. The mixture is also reported to have been effective in the treatment of liver abcesses caused by amoebic infection.

Diloxanide furoate (DLF) is described in the *Indian Pharmacopoeia* [1] and in the BP [2] whereas metronidazole (MNZ) is described both in these pharmacopoeias and the USP [3]. Colorimetric methods have been reported for DLF [4]. MNZ has been determined colorimetrically [5–7], polarographically [8], by gas chromatography [9, 10] and by HPLC [11, 12]. There is only one report for the analysis of the mixture by HPLC [13].

The present work represents an attempt to develop a simple yet inexpensive spectrophotometric method that can be adapted easily in drug control laboratories for the simultaneous determination of both compounds.

Experimental

Reagents and equipment

Diloxanide furoate and metronidazole reference compounds were obtained from the Central Drugs Laboratory, Calcutta, India, and used without further purification. All inorganic and organic chemicals were of analytical reagent grade.

A Beckman UV-visible spectrophotometer Model-24 equipped with a recorder was used for all UV measurements.

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Commercial samples of the mixture were obtained from the manufacturers and from local markets.

Method

An accurately weighed quantity of powdered tablets equivalent to about 100 mg of diloxanide furoate was placed in a 100-ml volumetric flask. A 25 ml volume of methanol was added to dissolve the medicament and the solution was diluted to 100 ml with water. The resulting suspension was filtered and 10 ml of the filtrate was further diluted to 100 ml with 0.01 M sodium hydroxide. A 5 ml sample of the resultant solution was diluted to 50 ml with 0.01 M sodium hydroxide. The absorbance of this solution was measured in a 1-cm silica cell at 247 and 320 nm using 0.01 M sodium hydroxide as a blank.

Calculations were done using the following equations:

$$\text{Weight (mg) of diloxanide furoate} = 134.4\ A_{247} - 37.3\ A_{320} \quad (1)$$

$$\text{Weight (mg) of metronidazole} = 188.7\ A_{320} - 3.8\ A_{247}. \quad (2)$$

The usual ratio of diloxanide furoate and metronidazole is 5:4. It was therefore desirable to determine the ratios within which one of them can be accurately determined in the presence of the other compound. Table 1 shows results of experiments conducted with different ratios of the mixture when one of them is kept constant and vice versa; the recoveries are well within the limits of experimental error.

Table 1
Recovery experiments from authentic samples of diloxanide furoate (DLF) and metronidazole (MNZ) in different ratios

	Ratio		Recoveries* (Mean ± SD)	
Sample No.	DLF	MNZ	DLF	MNZ
1	5.0	: 3.0	99.5 ± 0.40	101.2 ± 0.07
2	5.0	: 3.5	99.8 ± 0.66	101.0 ± 0.14
3	5.0	: 4.0	99.0 ± 0.41	101.1 ± 0.15
4	5.0	: 4.5	100.4 ± 0.12	102.2 ± 0.06
5	5.0	: 5.0	100.7 ± 0.31	102.0 ± 0.30
6	4.0	: 4.0	99.9 ± 0.04	101.4 ± 0.15
7	4.5	: 4.0	100.1 ± 0.16	102.1 ± 0.19
8	5.5	: 4.0	100.0 ± 0.17	101.3 ± 0.58
9	6.0	: 4.0	100.7 ± 0.44	102.4 ± 0.37

*$n = 5$.

Experiments were also conducted with standard additions to one of the commercial samples. Table 2 shows that the recoveries are well within experimental error.

The method was also applied to several commercial samples. The results are given in Table 3.

Results and Discussion

In the analysis of binary mixtures, Vierordt's method [14] is generally applied. In such cases, it is essential to select two points on the wavelength scale where the ratios of

Table 2
Recovery experiments on standard additions to a commercial sample*

	Diloxanide furoate		Metronidazole	
Sample no.	Added (mg/tablet)	Recovery† (%)	Added (mg/tablet)	Recovery‡ (%)
1	24.63	99.6	—	—
2	49.25	99.0	—	—
3	73.88	98.8	—	—
4	98.50	100.3	—	—
5	123.13	100.3	—	—
6	—	—	24.95	98.2
7	—	—	49.90	101.2
8	—	—	74.85	99.5
9	—	—	99.80	100.7
10	—	—	124.75	98.4

*Entamizole tablets. Declared content: diloxanide furoate 250.0 mg, metronidazole 200.0 mg. Found: Diloxanide furoate 241.3 mg, 196.0 mg metronidazole.
†Mean recovery (±SD) of diloxanide furoate = 99.59 ± 0.69%.
‡Mean recovery (±SD) of metronidazole = 99.6 ± 1.34%.

absorptivities are maxima. The most suitable wavelengths for mixtures of diloxanide furoate and metronidazole would be 247 and 320 nm, respectively (Fig. 1). The measured absorptivities (A 1%, l_{cm}) of diloxanide furoate at 247 and 320 nm are 748 and 15, respectively, whereas those of metronidazole are 148 and 533. These values were obtained from standard solutions of diloxanide furoate and metronidazole in 0.01 M sodium hydroxide. The figures given in equations (1) and (2) were obtained by numerical substitution for the absorptivity values of equations (3) and (4), taking into consideration the dilution factor in the procedure.

$$\text{Concentration of diloxanide furoate} = (A_2\beta_2 - A_2\beta_1)/(\alpha_1\beta_2 - \alpha_2\beta_1) \quad (3)$$

$$\text{Concentration of metronidazole} = (A_2\alpha_1 - A_1\alpha_2)/(\alpha_1\beta_2 - \alpha_2\beta_1) \quad (4)$$

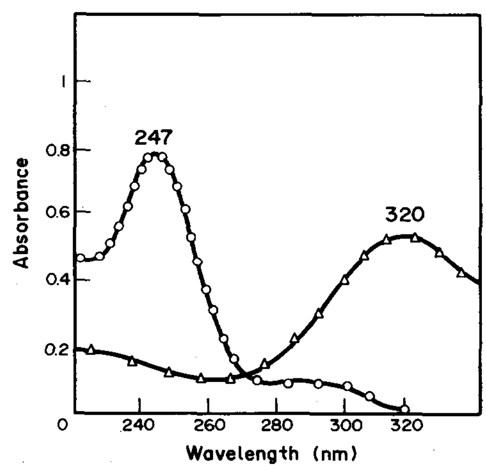

Figure 1
UV spectra of 0.001% (w/v) solution of diloxanide furoate (-O-O-O-) and metronidazole (-Δ-Δ-Δ-) in NaOH (0.01 M).

Table 3
Results obtained with commercial samples

Sample no.	Diloxanide furoate: Declared content (mg/tablet)	Diloxanide furoate: Found§ (% of declared content (±SD))	Metronidazole: Declared content (mg/tablet)	Metronidazole: Found§ (% of declared content (±SD))
1*	250.0	96.5 ± 0.68	200.0	98.0 ± 0.73
2*	250.0	101.2 ± 0.36	200.0	96.5 ± 0.52
3*	250.0	99.1 ± 0.54	200.0	99.0 ± 0.74
4*	250.0	103.5 ± 0.97	200.0	98.5 ± 0.62
5*	250.0	102.7 ± 0.57	200.0	97.5 ± 0.85
6*	250.0	103.5 ± 0.63	200.0	95.8 ± 0.61
7†	250.0	95.4 ± 0.59	200.0	99.1 ± 0.43
8‡	500.0	99.0 ± 1.10	400.0	101.5 ± 0.78
9‡	500.0	98.3 ± 0.92	400.0	102.5 ± 0.89
10‡	500.0	99.5 ± 0.83	400.0	101.8 ± 0.89
11‡	500.0	98.6 ± 0.76	400.0	101.4 ± 0.46
12‡	500.0	98.7 ± 0.69	400.0	103.5 ± 0.52

*Entamizole tablets (Boots, Bombay, India).
†Dyrade-M tablets (Cipla, Bombay, India).
‡Metrogyl compound tablets (Ifiunik, Bombay, India).
§$n = 5$.

where A_1 and A_2 are absorbance values of the mixture at 247 and 320 nm, respectively; α and β represent the absorptivities of diloxanide furoate and metronidazole, respectively, at the relevant wavelengths.

It was found that absorption of carbon dioxide results in reduction of the assay values for diloxanide furoate. However, for metronidazole there was no change. It is therefore desirable that a fresh solution of 0.01 M sodium hydroxide should be used.

From the data it is seen that the method is not only fast, simple and sensitive but also gives reproducible results.

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