Indian Journal of Chemical Technology
Vol. 13, January 2006, pp.81-83

Simultaneous spectrophotometric determination of formoterol fumarate and budesonide in their combined dosage form

A V S S Prasad

Department of Chemistry, National Institute of Technology, Warangal 506 004, India
Email: avssprasad@rediffmail.com

Received 4 January 2005; revised received 21 June 2005; accepted 6 October 2005

A new UV spectrophotometric method for the simultaneous determination of formoterol fumarate and budesonide in their combined dosage form has been developed. The λ_{max} values for formoterol fumarate and budesonide in methanol medium were found to be 217 nm and 252 nm respectively. The results of analysis by this method have been found to be precise and accurate.

Keywords: Simultaneous determination, Formoterol fumarate, Budesonide, Combined dosage form
IPC Code: Int. Cl.[7] G01J3/00

Formoterol fumarate (FF) is an antiasthamatic drug and its chemical name is formamide, *N*-[2-hydroxy-5-[(1R)-1-hydroxy-2-[[(1R)-2-(4-methoxyphenyl)-1-methyl ethyl]-amino]ethyl]phenyl-, res-, (2E)-2-butenedioate] (2:1) salt. Budesonide (BD) is an anti-inflammatory drug and its chemical name is (11β,16α)-16,17-[butylidene bis(oxy)-11,21-dihydroxypregna-1,4-diene-3,20-dione]. A combination of formotorol fumarate and budesonide is commonly used in the treatment of persistent asthma. Although a few methods have been reported in the literature for the determination of FF[1-4] alone and BD[1,5,6] alone, no method has been reported for the simultaneous spectrophotometric determination of these two drugs in a mixture. The present communication deals with the development of a simple and rapid UV spectrophotometric method for the simultaneous determination of FF and BD in their combined dosage form.

Experimental Procedure

Instrument

Shimadzu UV-160, a UV-Visible double beam spectrophotometer with matched quartz cells of pathlength 1 cm was used for all spectral and absorbance measurements.

Solvent

The solubility of both the drugs was tested in different solvents, *viz.* water, methanol, acetone and benzene (Qualigens). It was found that both the drugs are soluble in methanol. Hence, the present study was conducted in methanol.

Standard stock solutions for bulk drugs

Standard stock solution of FF (30 μg/mL, Cipla, 98% pure) was prepared by dissolving 3 mg of pure FF in 100 mL of methanol and the standard stock solution of BD (500 μg/mL, Cipla, 98% pure) was prepared by dissolving 50 mg of pure BD in 100 mL of methanol. These solutions were used for the preparation of calibration curves.

Standard stock solution of FF and BD mixture (30 μg/mL of FF and 500 μg/mL of BD) was prepared by dissolving 3 mg of pure FF and 50 mg of pure BD in 100 mL of methanol. This solution was used for the determination of FF and BD in the mixture.

Calibration curves

For the preparation of calibration curves, aliquots of standard stock solution of FF or BD in the range of 0.5-2.5 mL were delivered into a series of 10 mL calibrated tubes and the volume in each tube was made upto 10 mL with methanol. The diluted standard solution of each drug was scanned separately keeping methanol as blank. The λ_{max} values for FF and BD were found to be 217 and 252 nm, respectively. The absorbances of the standard solutions of both FF and BD were recorded against methanol at both the wavelengths and the respective calibration curves were prepared.

Determination of FF and BD in bulk drug mixture

For the determination of FF and BD in the bulk drug mixture, aliquots of the standard stock solution (0.5-2.5 mL) containing both FF (30 μg/mL) and BD (500 μg/mL) were delivered into a series of 10 mL calibrated tubes and the volume in each tube was made upto to 10 mL with methanol. The absorbances were recorded against methanol at 217 and 252 nm. The amounts of FF and BD present in the bulk drug mixture were determined by using simultaneous equations.

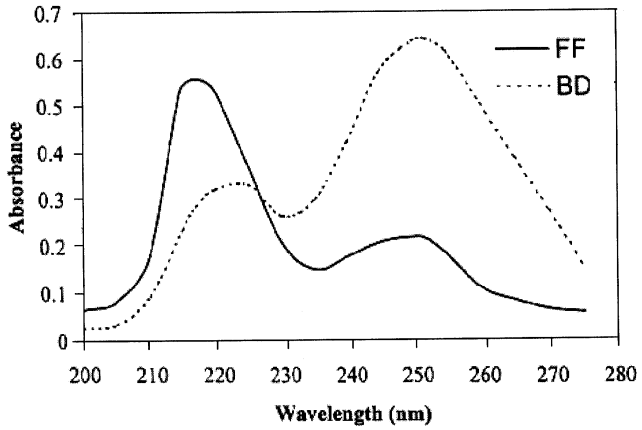

Fig. 1—UV spectra of FF (1.303×10^{-5}M) and BD(5.806×10^{-5}M) in methanol

Determination of FF and BD in combined dosage forms

For the determination of FF and BD in the combined dosage forms (which are commercially available as rotacaps), twenty combined dosage forms each with labeled amounts of 6 mg of FF and 100 mg of BD were weighed. They were opened and the contents were emptied into a small beaker and mixed thoroughly. The empty shells of the combined dosage forms were weighed and the amount of the combined dosage forms powder was determined by the difference. The additives used in the preparation of combined dosage forms such as talc, starch, boric acid, stearic acid, magnesium stearate, kaolin, sodium lauryl sulphate and gelatin may interfere in the determination of FF and BD. Therefore FF and BD were separated by extracting them from the combined dosage form with isopropanol in the preliminary step. Hence, an accurately weighed rotacap powder equivalent to the mixture of 60 μg of FF and 1000 μg of BD was taken and extracted with isopropanol and filtered. The filtrate was evaporated to dryness and the residue was dissolved in 10 mL of methanol. The absorbances of this solution were recorded against methanol at both 217 and 252 nm. The amounts of FF and BD present in the combined dosage form were determined by using simultaneous equations.

Results and Discussion

Since FF and BD are available in combined dosage forms, it is clear that, no chemical reaction takes place between these two drugs. Hence, simultaneous spectrophotometric determination method for the determination of individual drugs in a mixture[7] can be applied for their determination in their combined dosage forms. It was observed that FF absorbs strongly at a wavelength of 217 nm and weakly at 252 nm while BD absorbs strongly at 252 nm and weakly at 217 nm in methanol medium. Since both the drugs show absorbance at both the wavelengths in the mixture (Fig. 1), the absorbance obtained at each wavelength is the sum of the absorbances of each of the drugs at that particular wavelength. The following two equations follow

$$_{217}A_M = {}_{217}A_{FF} + {}_{217}A_{BD} \quad ...(1)$$
$$_{252}A_M = {}_{252}A_{FF} + {}_{252}A_{BD} \quad ...(2)$$

where A_M represents the absorbance of the mixture, while A_{FF} and A_{BD} represent the absorbance of the respective pure drugs. Here, $A=\varepsilon bC$, where ε is the molar absorptivity at a given wavelength (217 or 252 nm), C is the concentration (mol/L) and b is the thickness or the length of absorbing medium (cm). If b=1 cm then, the above two equations become

$$_{217}A_M = {}_{217}\varepsilon_{FF}\, C_{FF} + {}_{217}\varepsilon_{BD}\, C_{BD} \quad ...(3)$$
$$_{252}A_M = {}_{252}\varepsilon_{FF}\, C_{FF} + {}_{252}\varepsilon_{BD}\, C_{BD} \quad ...(4)$$

Solution of the simultaneous Eqs (3) and (4) gives

$$C_{FF} = ({}_{252}\varepsilon_{BD}\,{}_{217}A_M - {}_{217}\varepsilon_{BD}\,{}_{252}A_M)/({}_{217}\varepsilon_{FF}\,{}_{252}\varepsilon_{BD} - {}_{217}\varepsilon_{BD}\,{}_{252}\varepsilon_{FF}) \quad ...(5)$$
$$C_{BD} = ({}_{217}\varepsilon_{FF}\,{}_{252}A_M - {}_{252}\varepsilon_{FF}\,{}_{217}A_M)/({}_{217}\varepsilon_{FF}\,{}_{252}\varepsilon_{BD} - {}_{217}\varepsilon_{BD}\,{}_{252}\varepsilon_{FF}) \quad ...(6)$$

From the respective calibration curves, the molar absorptivities of FF at 217 and 252 nm are found to be 4.296×10^4 and 1.671×10^4 L mol^{-1} cm^{-1}, respectively and the molar absorptivities of BD at 217 and 252 nm are found to be 4.959×10^3 and 1.106×10^4 L mol^{-1} cm^{-1}, respectively. By using the absorbances of the bulk drug mixture (or combined dosage forms) at both the wavelengths, the concentrations of FF and BD are calculated.

Analytical data

At the first stage of the method, the concentration range of FF alone and BD alone was fixed and the calibration curves for both the drugs at both the wavelengths were prepared. Molar absorptivity and Sandell's sensitivity for FF alone and BD alone were calculated at their respective wavelengths. Least square regression analysis was carried out to obtain the slope, the intercept and the correlation coefficient values. The precision of the proposed method was ascertained from the absorbance values obtained by the determination of six replicates of a fixed amount of pure FF and pure BD in their respective solutions

Table 1— Optical characteristics, precision and accuracy of the proposed method

Parameters	FF	BD
λ_{max} (nm)	217	252
Concentration range (μg/mL)	1.5-7.5	25-125
Optimum photometric range	1.8-7.2	23.9-122.6
Molar absorptivity (L mol^{-1} cm^{-1})	4.296×10^4	1.106×10^4
Sandell's sensitivity (μg cm^{-2}/0.001 absorbance unit)	0.107	0.384
Regression equation (y)*		
Slope (*b*)	0.932	0.205
Intercept (*a*)	0.003	0.019
Correlation coefficient (*r*)	0.9999	0.9998
Relative standard deviation (%) **	0.418	0.748

*$y = a + bc$, where c is the concentration in μg/mL and y is the absorbance unit.
**For six replicate samples.

Table 2—UV spectrophotometric determination of FF and BD in their combined dosage form

Combined dosage forms*	Labeled amount (mg)		% Recovery (mg)			
			Proposed method**		Reference method	
	FF	BD	FF	BD	FF[4]	BD[6]
Rotacaps-1	6	100	99.00	99.02	100.90	98.76
Rotacaps-2	6	100	98.83	99.06	100.90	98.76
Rotacaps-3	6	100	99.50	100.96	100.90	98.76

*Different batches of a pharmaceutical company.
**Average of six determinations.

(60 μg/mL for FF and 1000 μg/mL for BD). The percent relative standard deviation values were calculated for FF and BD at their respective wavelengths. The results are given in Table 1.

At the second stage of the method, the absorbances at both the wavelengths were recorded and the amounts of FF and BD in the bulk drug mixture were determined using simultaneous equations.

At the third stage of the method, commercial formulations (combined dosage forms in the form of rotacaps) containing FF and BD were analyzed by the proposed method and the amounts of each drug in combined dosage form were determined. The application of the proposed method to the commercial formulations was verified by means of replicate determinations of FF and BD in combined dosage forms. The average values of determined amounts of FF and BD in combined dosage forms are given as percent recoveries in Table 2. These results are very close to labeled amounts of FF and BD in combined dosage forms. The results obtained by the proposed method were compared with the results of individual reference methods for FF[4] and BD[6]. All the results are summarized in Table 2. The results show the applicability of the method to determine the quantity of FF and BD in combined dosage forms.

Conclusion

The proposed UV spectrophotometric method for the simultaneous determination of FF and BD is accurate and of good precision. It is simple, rapid and does not require stringent conditions or costly solvents. It is, therefore, applicable for the micro determination of FF and BD in pure and combined dosage form in quality control laboratories.

Acknowledgement

The author is grateful to M/s Cipla Manufacturing and Research Division, Mumbai for providing pure samples of both the drugs.

References

1 Reynolds J E F, *Martindale the Extra Pharmacopoeia*, 29th edn (The Pharmaceutical Press, London), 1989, 1572, 885.
2 Vandenbeers B T J, Portier E J G, Vandenbeers M, Bharat M C P & Vanboxtel C J, *Ther Drug Monit*, 16 (1994) 196.
3 Kamimura H, Sasaki H, Higuchi S & Shiobara Y, *J Chromatogr*, 229 (1982) 337.
4 Seng J Z, Chen J, Tian S J & Sun Z P, *J Pharm Biomed Anal*, 21(3) (1999) 569.
5 Roth G, *J Pharm Sci*, 69 (1980) 766.
6 Krzek J, Hubicka U, Dabrowska M & Leciejewicz E, *Chromatographia*, 56(11) (2002) 759.
7 More H N, Mahadik K R & Kadem S S, *Indian Drugs*, 36 (1999) 144.