Spectrometric Determination of Formoterol Fumarate in Rotacap Formulation

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A new simple, sensitive spectrometric method was developed on the basis of a colour reaction of formoterol with diazotised p-nitroaniline. The method is based on formation of yellow chromophore which has an absorption maxima at 398 nm and obeys Beer's law in the concentration range of 1-40 μg/ml. Results of the analysis were statistically validated by recovery studies. The method was found to be suitable for routine determination of formoterol fumarate in rotacap formulation.

Chemically, formoterol fumarate[1] is (±)-N-[2-hydroxy-5-{(1-hydroxy-2-[[2-(4-methoxyphenyl)-1-methylethyl]amino]-ethyl}phenyl] formamide. It is a potent β-2 agonist and is used in asthma therapy with maximum dose of 12 μg/rotacap[2]. Literature survey reveals that the drug is determined using HPLC[3,4], GC derivatization[5] and capillary electrophoresis[6] methods. In the present study, the presence of the phenolic group in formoterol was exploited for a coupling reaction with diazotised p-nitroaniline.

A Shimadzu UV/Vis spectrophotometer (UV-1601) with 1 cm matched quartz cell was used. A standard solution of formoterol fumarate was prepared by dissolving 10 mg of formoterol fumarate in 1.5 ml of 10% hydrochloric acid. The volume was made up to 10 ml with distilled water to get a concentration of 1000 μg/ml.

One percent w/v p-nitroaniline solution was prepared by dissolving 1 g of p-nitroaniline in 10 ml of concentrated hydrochloric acid followed by the addition of 50 ml of distilled water. The solution was boiled, cooled and filtered. The volume of the filtered solution was made up to 100 ml with distilled water. One percent w/v sodium nitrite, 10%v/v hydrochloric acid and 1% w/v sodium hydroxide solution were freshly prepared in distilled water.

To 1.5 ml of p-nitroaniline, 1.5 ml of sodium nitrite and 2.0 ml of hydrochloric acid were added. The diazotised mixture was poured into a mixture of aliquots of 0.1, 0.2, 0.3, 0.4 ml of standard solution of formoterol fumarate and 1.0 ml of sodium hydroxide solution. The volume was made up to 10 ml with distilled water. The absorbance of the yellow coloured chromophore was measured at 398 nm against reagent blank. The method was validated for fixing optimum concentration and volume required for maximum absorbance, stability of colour and order of mixing. The accuracy and reliability of the method was proved through recovery studies.

The method was extended for determination of formoterol fumarate from rotacap formulation, strength 12 μg per rotacap, Foratec (Protec, Mumbai). A total of 20 rotacaps were weighed, powdered and dissolved in a mixture of 1 ml of sodium hydroxide and 4 ml of distilled water. The solution was filtered through sintered glass funnel into a 10 ml volumetric flask. Diazotised p-nitroaniline solution prepared by mixing 1.5 ml of 1%w/v p-nitroaniline, 1.5 ml of 1% w/v of sodium nitrite and 2 ml of 10%v/v hydrochloric acid was added to alkaline formoterol fumarate solution. The solution was mixed well and the absorbance of the yellow coloured chromophore was measured at 398 nm against reagent blank. The results of the assay are recorded in Table 1.

Recovery studies were carried out at two different levels by adding 100 and 150 μg of pure drug (0.1 and 0.15 ml standard stock solution) to previously analyzed two separate batches of rotacap formulation solution. From the amount of total drug found, percentage recovery was calculated. The results are presented in Table 1.

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TABLE 1: ASSAY OF ROTACAP FORMULATION AND RECOVERY STUDIES.

Trial Bt. No.*	Assay		Recovery study			
	Label amt. μg/ rotacap	Amount found (20 rotacaps μg and %content)**	Amt. added (μg)	Total found μg**	Amount of standard recovered μg	% recovery
B- I	12	236 (98.3)	100	335	98.6	98.6
B-II	12	237.2 (98.8)	150	390	152.6	101.7

*The rotacaps of two separate batches obtained from the same manufacturer were analyzed. ** Average of 6 observations.

The Beer's law was obeyed in the concentration range of 1-40 μg/ml, molar absorptivity determined to be $2.26X10^{5}$ l/mole.cm and Sandell's sensitivity 0.0707 μg/cm^2-0.001 absorption units. The regression equation (Y=a+bx) was obtained by a linear least squares treatment of the results, established slope as 0.012686 and intercept 0.0672 with standard deviation of 0.16 and coefficient of variation 0.10. The data from recovery studies indicated no interference of excipients present in the formulation. The developed method was thus found to be sensitive, accurate, precise and reproducible and can be used for the routine determination in rotacap formulation.

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Concurrent Assay of Metformin and Glimepiride in Tablets Using RP-HPLC with Wavelength Programming

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A rapid assay procedure based on RP-HPLC has been developed for the simultaneous determination of metformin and glimepiride in dosage form. The HPLC determination was carried out on a μBondapak C_{18} (300x3.9 mm) 10 μm with use of a flow rate of 1.0 ml/min. The programming regime

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