tio to form an intense yellowish green complex (plausibly II) showing λ_{max} at 360 nm has been made basis of the method, $2C_{11}H_{17}N_2O_2S.Na+Co^{2+} \rightarrow [(C_{11}H_{17}N_2O_2S)_2Co](II)+2\ Na^+$ for the sub-milligram level determination of the drug compound. Photometric titration of the drug compound with cobalt(II) are marked by a well-defined intersection at drug to reagent molar ratio of 2:1 in the form of an inverted L-shaped titration curve. It may be mentioned that the formation of above type of complex (II), as a result of the reaction of thiobarbitueric acid and related compounds such as thioureas with metal ions like cobalt (II) and copper (II) through coordination with sulphur atoms, is well known[10-12]. Further, these compounds as such are weak nucleophiles and their complexes with metal ions are not formed readily, triethylamine (a base) activates them by abstracting hydrogen from thiol sulphur thus making them strong nucleophiles. With this method, thiopentone sodium in the range 0.1-0.5 mg could be determined with a maximum RSD of 0.7%. The Recoveries of active ingredient content from drug formulation were in the range 99.0-99.6% with RSD's in the range 0.3-0.7% (Table I).

The proposed photometric titration methods besides being simple, are more sensitive than pharmacopoeic method[1]. The excellent solution stability of the reagents and that of colour as well as well-established stoichiometries of the colour reactions involved are other attractive features of the proposed methods.

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Simultaneous Spectrophotometric Estimation of Ibuprofen and Methocarbamol in Tablet Dosage Form

T. R. S. SATHEESHMANIKANDAN, DEEPA C. WALI, J. BARIWAL, S. S. KADAM AND S. R. DHANESHWAR*

Bharati Vidyapeeth Deemed University, Poona College of Pharmacy, Erandwane, Pune-411 038

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Two simple economical procedures for simultaneous estimation of ibuprofen and methocarbamol in two-component tablet formulation have been developed. The method employs Q-analysis and two-wavelength method. Ibuprofen has absorbance at 222 nm and methocarbamol has absorbance maxima at 224 nm and 272 nm. The isoabsorptive point of ibuprofen and methocarbamol was found to be 231.4 nm. Both

*For correspondence

E-mail: srdhaneswar@hotmail.com

drugs obeyed the Beer's law in the concentration ranges employed for these methods. The results have been validated statistically and by recovery studies.

Methocarbamol (MEC) is a centrally acting muscle relaxant[1]. It causes muscle relaxation without producing unconsciousness. Ibuprofen (IBU) is a propionic acid nonsteroidal antiinflammatory drug that possesses analgesic and antiinflammatory activity by reducing prostaglandin synthesis[2]. Fixed combination of IBU (400 mg) MEC (750 mg) is marketed as tablet formulation for treatment of acute muscle spasm along with inflammation. For MEC some HPLC[3-4] Methods have been reported. IBU is official in IP, USP and EP. Several methods for MEC that includes HPLC, spectrophotometry[5-6] have been reported in the literature for its assay. HPLC[7], GC[8], UV/Vis spectroscopy[9] and isocratic supercritical fluid chromatography[10] have been established for their simultaneous determination. The chromatographic methods that have been reported thus far proved to be uneconomical[11]. The present communication describes two simple, accurate, rapid, reproducible and economical methods for simultaneous spectrophotometric estimation of both these drugs in tablet dosage form.

A PC based Jasco V-530 recording spectrophotometer with spectral bandwidth of 2 nm and wavelength accuracy ±0.5 nm (with automatic wavelength correction) was employed for all measurements using a matched pair of 10 mm quartz cells. MEC (USP), IBU (IP), sodium hydroxide (Qualigen, Excel R, Mumbai) and double distilled water was used in present investigation. Stock solutions of IBU (100 μg/ml) and MEC (100 μg/ml) were prepared in 0.1 N sodium hydroxide. Each stock solution was suitably diluted to different concentrations and linearity was studied at respective wavelengths that were 222, 224, 272.4 and isoabsorptive point 231.4 nm.

In the quantitative assay of two components by Q analysis method[2,12,13], absorbances are measured at two wavelengths, one being the isobestic point and the other being the maximum absorption of one of the two components. From the overlain spectra of IBU and MEC absorbances were measured at two selected wavelengths, 231.4 nm (isobestic point) and 272.4 nm (wavelength of maximum absorption of MEC) as shown in fig. 1. The concentration of each component can be calculated by mathematical treatment of following equations which are: for IBU $C_1=Q_0-Q_2/Q_1-Q_2\times A/a$...(1) and for MEC $C_2=Q_0-Q_1/Q_2-Q_1\times A/a$...(2), where C_1 is the concentration of IBU, C_2 is the concentration of MEC, A is absorbance of sample at isobestic point wavelength (231.4 nm), a is absorptivity of IBU and MEC at isobestic wavelength, Q_1 is the ratio of absorbance of IBU at 272.4 nm to absorbance of IBU at 231.4 nm, Q_2 is the ratio of absorbance of MEC at 272.4 nm to absorbance of MEC at 231.4 nm and Qo is the ratio of absorbance of sample solution at 272.4 nm to absorbance of sample solution at 231.4 nm. Several mixed standards containing IBU and MEC in the concentration 4×n μg/ml and 7.5×n μg/ml (where n=1, 2... 6), respectively were prepared in 0.1N sodium hydroxide. By employing Eqns. 1 and 2, absorbance contributed by IBU and MEC to total absorbance at selected wavelength was worked out.

In the two-wavelength (absorbance difference) method[14], four wavelengths were selected for the estimation of IBU and MEC (fig 1). For the determination of IBU, two wavelengths were so selected that MEC showed same absorbance while IBU had different absorbance. For the determination of MEC two wavelengths were so selected that IBU showed same absorbance but MEC had different absorbance. The wavelengths selected for IBU were 234.8 and 272.4 nm and absorbance difference between these two points is A_1. For MEC the wavelengths selected were 239.5 and 264.8 nm and absorbance difference between these two points is A_2.

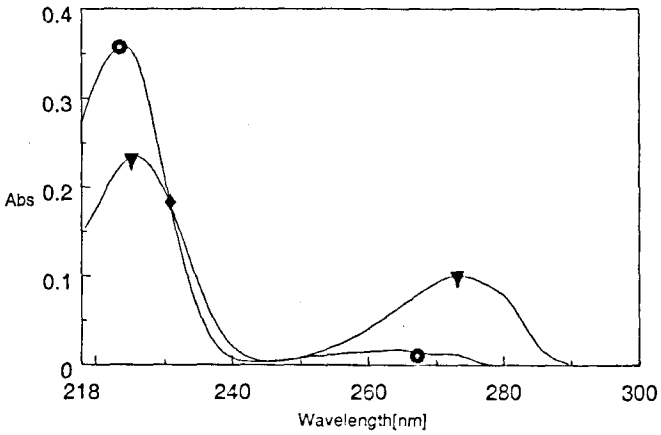

Fig. 1: Overlain spectra of MEC and IBU

Absorbance spectra obtained at different wavelengths in the range of 300-218 nm of MEC (▼), IBU (●) and isoabsorptive point. (◆) in 0.1 N sodium hydroxide overlain over each other.

TABLE 1: ANALYSIS OF STANDARD SAMPLES

Analyte	Method –I			Method –II		
	C.I.	SD	%SE	C.I.	SD	%SE
IBU	100.9 ± 1.40	1.3635	1.1568	100.8 ± 0.89	0.8433	0.9110
MEC	100.6 ± 0.80	0.7553	0.8638	100.9 ± 0.43	0.4080	0.6302

SD stands for standard deviation, % SE for percent standard error, C.I=R±ts/ün, where C.I. is confidence interval within which true value may be found at 95% confidence level, R stands for percent result of authentic samples or recovery, t is theoretical 't' values at 95% confidence level for n-1 degrees of freedom are t (0.05, 4)=2.776 and t (0.05, 5)=2.57 and n is the no of times the experiment repeated.

For each drug appropriate aliquots were pipetted out from standard stock solution in to a series of 10 ml volumetric flasks. The volume was made up to the mark to get solutions of concentrations of 4, 8, 12, 16 and 20 µg/ml for IBU and 7.5, 15, 22.5, 30 and 37.5 µg/ml for MEC. Calibration curve for IBU was constructed by plotting absorbance difference of IBU (A_1) against its concentration and calibration curve for MEC was constructed by plotting absorbance difference of MEC (A_2) against its concentration. By using quantitative mode of the instrument, intercept and slope values were obtained. Where 188.68 and 263.29 were the slope values of IBU and MEC, respectively, 0.063 and –0.075 were the intercept values of IBU and MEC respectively. The concentration of these two drugs was calculated by using the equations, $C_{MEC}=A_1*K+B$ ... (3), $C_{IBU}=A_2*K+B$ ... (4), where C_{MEC}=concentration of MEC, C_{IBU}= Concentration of IBU, K=intercept value of IBU and MEC, respectively and B=slope value of IBU and MEC, respectively. By applying the slope and intercept values so obtained, the concentration of IBU and MEC can be found out using the formula, $C_{MEC}=A_1*263.290-0.075$ (r=0.9998) and $C_{IBU}=A_2*188.679-0.063$ (r=0.9997).

Before analyzing the marketed formulations, the methods were validated by analyzing standard stock solutions mixed in the ratio 4:7.5 µg/ml and random samples prepared in the laboratory. The results of replicate determination (n=6) by both proposed methods were validated statistically and are shown in the Table 1.

Marketed tablet formulation (Ibugesic-M, methocarbamol–750+ibuprofen-400, Cipla) procured from a local pharmacy was analyzed using both the methods developed in this investigation. From the triturate of the 20 tablets an amount equivalent to 10 mg IBU was weighed and transferred to 100 ml volumetric flask, 0.1 N sodium hydroxide was added with intermittent shaking and the volume was made up to the mark with the same solvent. The solution was filtered through a Whatmann filter paper no 41. After appropriate dilutions the absorbances were measured and the concentration of each analyte was determined with the equation generated in both methods. The statistical data of the results obtained after replicate determination (n=6) are shown in the Table 2.

To study the recovery of IBU and MEC, different quantities of pure drugs (reference standards) were added to pre

TABLE 2: RESULTS OF ANALYSIS OF TABLET FORMULATIONS

Method	IBU		MEC	
	C.I	SD	C.I.	SD
M-1	100±1.1202	1.40	101 ± 0.6044	0.7553
M-2	101±0.6733	0.8415	101±0.3265	0.4081
M-R'	99±0.5143	0.6427	100.4±0.3022	0.3777

M-R' implies result obtained by reported methods[7], *each data represents results of six determinations in the analytical range (n=6)

TABLE 3: ANALYSIS OF RECOVERY EXPERIMENTS

Analyte	Method –I			Method –II		
	C.I.	SD	%SE	C.I.	SD	%SE
IBU	101.5 ± 1.02	0.9766	0.9740	100.9 ± 0.74	0.7009	0.8294
MEC	100.8 ± 1.32	1.2646	1.1153	101.4 ± 0.72	0.6818	0.8147

SD stands for standard deviation, % SE for percent standard error, C.I=R±ts/vn, where C.I. is confidence interval within which true value may be found at 95% confidence level, R stands for percent result of authentic samples or recovery, t is theoretical 't' values at 95% confidence level for n-1 degrees of freedom are t (0.05, 4)=2.776 and t (0.05, 5)=2.57 and n is the no of times the experiment repeated.

analyzed samples at a level of 50 to 150 percent but within the analytical concentration range of the proposed methods. The added quantities of individual drugs were estimated by both methods and the statistical data given in the Table 3 (n=5)

The proposed methods were found to be accurate, simple, economical, convenient and rapid for routine simultaneous estimation of IBU and MEC in tablet formulations. The modalities adopted in experimentation were successfully validated as per standard analytical procedures. Both the methods were validated by preliminary analysis of authentic laboratory samples and recovery studies. The results of analysis of authentic samples and the average recoveries obtained in each instance were compared with theoretical value of 100% by means of 't' test at a 95% confidence interval level. The recoveries obtained as indicated from Table1 for each drug do not differ significantly from 100% and there was no interference from common excipients used in the formulation indicating accuracy and reliability of both methods.

In the first method, calculations have been minimized by taking one of the measurements at an isoabsorptive point at 231.4 nm as ratio is fixed for specific mixture. The degree of dilution of two substances does not alter the Q-value within the limits of accurate absorptiometric measurements. Similarly second method is a very simple method and can be employed for routine analysis of these two drugs. Once the absorption difference values are determined, very little time is required for analysis, as it would only require determination of absorbencies of the sample solutions at four selected wavelength and few simple calculations.

The results of the analysis of commercial tablets were found to be satisfactory with standard deviation values within acceptable limits. Again both the methods are in well agreement with reported method[7], but with comparatively higher degree of precision as indicated from lower standard deviation values.

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