Experiments
Учебен експеримент в природните науки

SIMULTANEOUS ESTIMATION OF IBUPROFEN AND RANITIDINE HYDROCHLORIDE USING UV SPECTROPHOTOMETRIC METHOD

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Abstract. A new method has been developed for the simultaneous estimation of ibuprofen and ranitidine HCl using UV spectroscopy. The calibration graphs were linear in the ranges of 2-12 µg/ml for ibuprofen ($r^2 = 0.9994$) and 5-30 µg/ml for ranitidine HCl ($r^2 = 0.9992$). The values of limit of detection (LOD) and limit of quantification (LOQ) were determined 0.0196 and 0.0656 for ibuprofen and 0.0114 and 0.0379 for ranitidine HCl, respectively. RSD values for various determinations were found less than 1, which indicated good accuracy and precision of the method. The newly developed method was successfully applied for simultaneous estimation of two combination drugs, ibuprofen and ranitidine HCl in pharmaceutical tablets containing ibuprofen and ranitidine HCl.

Keywords: ibuprofen, ranitidine hydrochloride, simultaneous estimation, UV spectroscopy

Introduction

Ibuprofen, 2- (4- isobutyl– phenyl) propionic acid is a non-steroidal anti-inflammatory drug (NSAID) with a half-life of 1.8-2 h, and commonly used in the treatment of arthritis, post-operative and dental pain (Eiche et al., 2009; Issa et al., 2011; Hasnain & Nayak, 2012). Ibuprofen is used in the management of mild to moderate pain and inflammation in condition such as headache including migraine, postoperative pain, musculoskeletal and joint disorders such as alkylosing spondylitis, osteoarthritis and rheumatoid arthritis (Eiche et al., 2009). Ranitidine, N, N- dimethyl- 5- [2- (1- methyl amino- 2- nitro vinyl amino) ethyl thio methyl] furfuryl amine, is a H_2-antagonist with a half-life of 2.5-3h, which inhibits the gastric acid secretion and pepsin output (Grant, 1989). It is widely prescribed in active duodenal ulcers, gastric ulcers, Zollinger-Ellison syndrome, gastroesophageal reflux disease, and erosive esophagitis.[1)]

The literature survey reveals that some UV-spectrophotometric methods for estimation of ibuprofen (Benjamin et al., 2009; Gondalia, et al., 2010; Patel & Rajput, 2012) and for ranitidine (Raut & Sabnis, 1987; Haque et al., 2008; Salve et al., 2010) alone or combination with various drugs have been reported. However, any analytical method for

simultaneous estimation of ibuprofen with ranitidine hydrochloride is still not reported. In the present investigation, we made a plan to develop a simple method for simultaneous estimation of ibuprofen with ranitidine hydrochloride in pharmaceutical preparations using UV spectroscopy.

Experimental

Materials

Ibuprofen and ranitidine HCl were obtained from B. S. Traders Pvt. Ltd., India. All other chemicals and reagents used were of analytical grade.

Instrument

An UV-VIS Spectrophotometer (Thermo Spectronic UV-1, USA) with matched quartz cell corresponding to 1 cm path length and spectral bandwidth 1 nm was employed for simultaneous determination ibuprofen and ranitidine HCl.

Preparation of standard stock solution

Two standard stock solutions of 100 µg/ml were prepared for ibuprofen and ranitidine HCl after dissolving the 10 mg drugs in a 50 % v/v methanol solution and working standard solution of both drugs prepared on the day of analysis by suitable dilution of the stock solution with methanol.

Determination of maximum wavelength (λ_{max})

In this study, the stock solution of both drugs was carefully diluted with 50 % v/v methanol solution to 10 µg/ml of ibuprofen and ranitidine HCl. Then all samples were scanned separately in the range of 200-350 nm to detect λ_{max}s for ibuprofen and ranitidine HCl, separately.

Simultaneous equation method

The stock solution of both drugs were further diluted with 50 % v/v methanol solution to get a series of standard drug solution, i.e. 2-12 µg/ml for ibuprofen and 5-30 µg/ml for ranitidine HCl. Absorbances were measured at the selected wavelengths and absorptivities. Drugs were determined as mean of six independent determinations. Concentration in the sample was determined by using following equation (Dey et al., 2012):

$$C_x = (A_2 \,.\, ay_1 - A_1 \,.\, ay_2) \,/\, (ax_2 \,.\, ay_2 - ax_1 \,.\, ay_2)$$
$$C_y = (A_1 \,.\, ax_2 - A_2 \,.\, ax_1) \,/\, (ax_2 \,.\, ay_1 - ax_1 \,.\, ay_2)$$

where A_1 and A_2 = absorbance of mixture at 221 nm (λ_1) and 314 nm (λ_2), respectively; ax_1 and ax_2 = absorptivity of ibuprofen at λ_1 and λ_2, respectively; ay_1 and ay_2 = absorptivity of ranitidine HCl at λ_1 and λ_2, respectively; C_x = concentration of ibuprofen; C_y = concentration of ranitidine HCl.

Validation of method

Any newly developed method needs proper validation for its application in various respects**.** Here the method was validated in compliance with ICH guidelines (Dey et al., 2012). The following studies were performed for validation purpose.

Linearity: A linear relationship between absorbances and concentration was found for ibuprofen at concentration range of 2-12 µg/ml and ranitidine HCl at concentration range of 5-30 µg/ml, where 5 replicates of measurement were performed in each case.

Precision: The term precision is well required for any method validation and here it was determined by repeatability measurement and intermediate precision study, where measurement of absorbance was done by performing six replicates of measurement of same using a sample solution.

Recovery studies: In recovery studies, three different known concentration of standard drugs solution were added to the drug product as standard addition method. Therefore 8, 10, 12 µg/ml of ibuprofen and 16, 20, 24 µg/ml of ranitidine HCl were added to the dosage form that contained 10 µg/ml of Ibuprofen and 20 µg/ml HCl after proper sample dilution.

Limit of detection (LOD) and limit of quantification (LOQ): The LOD and LOQ study are extensively needed method validation in simultaneous estimation of various drugs in dosage form and these were calculated by taking the standard deviation of the y-intercept and slope of the calibration curve of selected drugs. The formula for determination of LOD and LOQ are given below:

$$\text{Limit of detection (LOD)} = 3\alpha / S$$

$$\text{Limit of quantification (LOQ)} = 10\alpha / S$$

where α is referred as standard deviation of y-intercept and S is referred as slope of the standard curve.

Robustness: Robustness is essential to detect the effect on absorbance in terms deliberate variation in the method parameter like wavelength (λ_1), pH and calculation of robustness is based on relative standard deviation of each parameter.

Determination of drug content in tablet containing ibuprofen and ranitidine HCl: The bi-layers tablets prepared by compressing the 400 mg of ibuprofen and 150 mg of ranitidine HCl along with suitable excipients using 12 mm flat punches. 20 tablets were taken and crushed in a pestle and mortar. The accurately weighed powder sample equivalent to 400 mg ibuprofen and 150 mg of ranitidine HCl was subjected to a 100 ml volumetric flux and diluted followed by sonication with 50 % v/v methanol solution to dissolve the sample. The solution was then filtered through Whatmann® filter paper (No. 40) and 0.1 ml filtrate was further diluted with same diluting solution and analyzed by multicomponent mode of analysis in a UV-VIS spectrophotometer (Thermo Spectronic UV-1, USA), where 50 % v/v aqueous methanol solution was used as blank.

Results and discussion

An UV-spectrophotometric method was developed for simultaneous estimation of ibuprofen and ranitidine HCl in tablet dosage form. The λ_{max}s were found to be 221 nm for the ibuprofen and 314 nm ranitidine HCl in 50% v/v aqueous methanol solution as solvent. An overlaid spectrum was shown in Fig. 1.

Linearity

Linearity generally depends on the correlation coefficient (r^2) between the absorbance with its respective concentrations. In this investigation, r^2 was found to be 0.9994 for ibuprofen and 0.9992 for ranitidine HCl. The r^2 values were obtained from calibration curve constructed in the concentration range of 2-12 µg/ml for ibuprofen and 5-30 µg/ml for ranitidine HCl shown in Table 1.

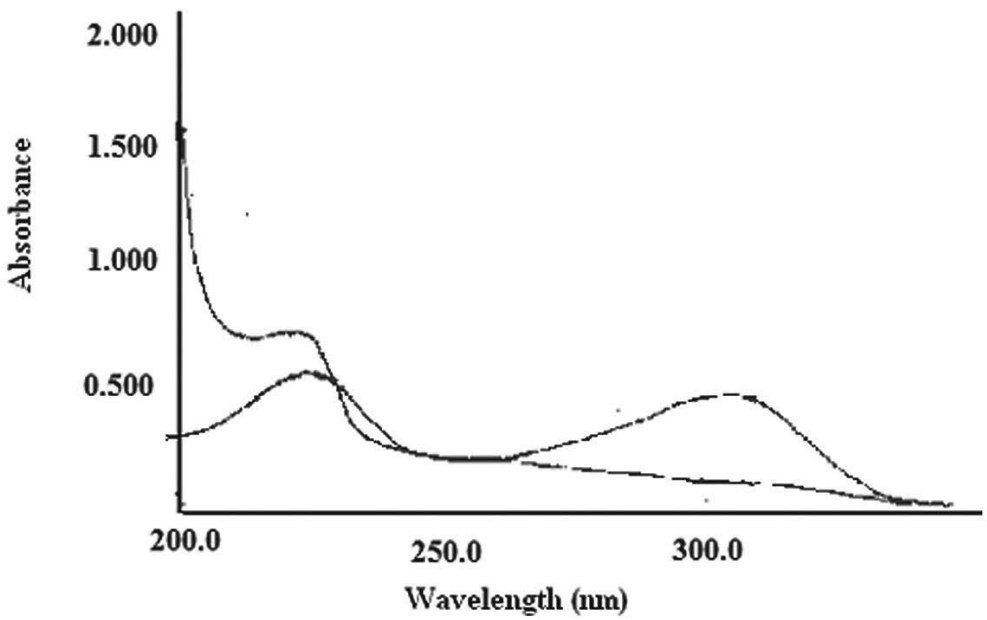

Fig. 1. Overlaid spectra of ibuprofen and ranitidine hydrochloride

Precision

Precision determined in terms of repeatability and intermediate precision studies were expressed as relative standard deviation (RSD) of the absorbance. The results represented

the repeatability, intra-day and inter-day variation in absorbance at concentration of 10 µg/ml for ibuprofen and 20 µg/ml for ranitidine HCl and these values were found within the acceptable range (less than 1 % for both drugs shown in Table 1).

Table 1. Summary of linear regression and validation data

Parameters*	**Ibuprofen**	**Ranitidine HCl**
Wavelength (nm)	222.0 nm	314.0 nm
Linearity range(µg/ml)	2-12	5-30
Linear regression equation	Y = 0.0381+ 0.0015	Y = 0.0633 - 0.0025
Slope ± SD	0.0381 ± 0.00035	0.0633 ± 0.00033
Intercept ± SD	0.0015 ± 0.00025	0.0025 ± 0.00024
Correlation coefficient (r^2)	0.9994	0.9992
Limit of detection (LOD)	0.0196	0.01147
Limit of quantification (LOQ)	0.0656	0.0379
Repeatability (RSD)	0.582	0.352
Intra-day (RSD)	0.442	0.376
Inter-day (RSD)	0.531	0.341

* Represents average of six estimations (n = 6)

Recovery studies

The recovery studies were performed taking the concentration level at 80, 100 and 120 % for test samples as per ICH guidelines. The percentage recovery all the three levels are shown in Table 2 and results were found satisfactory. The percentage recovery was laid in range between 0.443 to 0.531 for ibuprofen and 0.376 to 0.341 for ranitidine HCl.

Table 2. Recovery studies (standard addition method)

Drug	**Recovery level (%)**	**Initial amount (µg/ml)**	**Amount added (µg/ml)**	**% Recovery***	**% RSD***
Ibuprofen	80	20	16	98.19 ± 0.16	0.160
	100	20	20	98.25 ± 0.15	0.152
	120	20	24	98.60 ± 0.28	0.286
Ranitidine HCl	80	20	16	98.76 ± 0.11	0.106
	100	20	20	98.95 ± 0.09	0.090
	120	20	24	99.49 ± 0.40	0.404

* Represents average of three estimations (n = 3)

Limit of detection (LOD) and limit of quantification (LOQ)

The values of LOD and LOQ were determined 0.0196 and 0.0656 for ibuprofen and 0.0114 and 0.0379 for ranitidine HCl, respectively, that confers the sensitivity of developed method.

Table 3. Robustness study of variation in method parameters

Drug	Parameters		Conc. used (µg/ml)	Mean* conc. obtained (µg/ml)	SD*	%RSD*
Ibuprofen	Wavelength (λ)	223 nm	10	9.90	0.21	0.207
		221nm	10	9.96	0.09	0.091
		219 nm	10	9.88	0.21	0.216
	pH	1.4	10	9.85	0.20	0.197
		1.2	10	9.94	0.08	0.081
		1.0	10	9.81	0.19	0.195
Ranitidine HCl	Wavelength (λ)	316 nm	20	19.74	0.21	0.210
		314 nm	20	19.91	0.11	0.109
		312 nm	20	19.82	0.21	0.212
	pH	1.4	20	19.84	0.19	0.187
		1.2	20	19.94	0.08	0.084
		1.0	20	19.86	0.20	0.197

Robustness

Table 3 represents that all the values for robustness in developed method were found less than 1 % (RSD values) and assure the robustness of method.

Determination of drugs content in tablets containing ibuprofen and ranitidine HCl

The prepared bi-layered tablets containing 400 mg of ibuprofen and 150 mg ranitidine HCl was assayed using the developed method. The assay results of tablets are displayed in Table 4. The RSD values less than 1 % concludes that the developed method is accurate and precise.

Table 4. Analysis of drug content in tablet containing ibuprofen and ranitidine hydrochloride

Drug	Label claim	% Mean assay*	SD*	% RDS*
Ibuprofen	400 mg	101.09	0.23	0.226
Ranitidine HCl	150 mg	100.66	0.55	0.544

Conclusion

The developed method was found simple, rapid and permit direct and simultaneous determination of ibuprofen and ranitidine HCl. RSD values for various determinations were found less than 1, which indicated good accuracy and precision of the method. Moreover, the new method is used for the determination of the two combination drugs, ibuprofen and ranitidine HCl in pharmaceutical preparation, where several excipients are present.

NOTES

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