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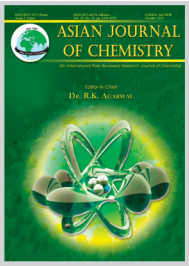

Simultaneous Estimation of Thiocolchicoside and Diclofenac Potassium in Tablet Formulation by UV Spectrophotometry

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A simple, specific, accurate, precise and reproducible method has been developed and validated for the simultaneous estimation of thiocolchicoside and diclofenac potassium in pharmaceutical formulation by UV-spectrophotometry, which includes simultaneous equation method (**method A**) and absorbance ratio method (**method B**). For the development of **method A**, wavelengths were selected as 260 nm λ_{max} for thiocholchicoside and 277 nm λ_{max} for diclofenac potassium, while for **method B**, 277 nm λ_{max} was selected for the diclofenac potassium and 266 nm was the isoabsorptive point of thiocholchicoside and diclofenac potassium. Both drugs follow Beer-Lambert's law at the selected wavelengths in concentration range of 5-25 µg/mL for thiocholchicoside and 5-25 µg/mL for diclofenac potassium. The per cent recoveries of the drugs were found to be nearly 100 % representing the accuracy of both the methods. Validation of the proposed methods was carried out for its accuracy, precision and ruggedness according to ICH guidelines. The proposed methods can be successfully applied in routine work for the determination of thiocholchicoside and diclofenac potassium in a combined dosage form. Also, the **method B** can be applied for estimation of thiocholchicoside even in presence of the diclofenac potassium in the formulation matrices without interference.

Key Words: Thiocolchicoside, Diclofenac potassium, Absorbance ratio method, Simultaneous equation method.

INTRODUCTION

Thiocolchicoside (TCH) is (s)-N-[3-(β-D-glucopyranoxy-loxy)-5,6,7,9- tetrahydro-1,2 dimethoxy-10-(methylthio)-9-oxobenzo[a]heptalen-7yl] acetamide. It is an antiinflammatory analgesic agent with muscle relaxant action[1]. Literature survey reveals that for the simultaneous determination of thiocolchicoside with other drugs spectrophotometric[2], HPTLC[3] and HPLC methods[4,5] were reported. Diclofenac potassium (DIC) is potassium [*o*-(2,6-dichloroanilino)phenyl] acetate[6]. It is a non-steroidal antiinflammatory and analgesic, agent based in reducing pain in conditions such as arthritis or acute injury. Literature survey also reveals the spectrophotometric determination of diclofenac in the presence of cyclodextrin[7], high performance thin layer chromatographic method for the determination of diclofenac potassium in pharmaceutical formulation[8], high performance liquid chromatographic determination of diclofenac in human plasma after solid-phase extraction[9] and stability indicating HPLC method for simultaneous determination of mephenesin and diclofenac diethylamine[10]. To the best of our knowledge, there is no other method reported for the estimation of thiocolchicoside and DIC in combined dosage form. The present work describes a simple, accurate and precise method for simultaneous estimation of thiocolchicoside and diclofenac potassium in combined dosage form by two simple UV spectrophotometric methods.

EXPERIMENTAL

Shimadzu double beam UV-visible spectrophotometer (model 1700) with 1 cm matched quartz cuvettes were used for all absorbance measurements. Citizen digital balance was used for weighing the samples. All the chemicals and reagent used were of AR grade. Double distilled water and Whatman filter paper (no. 41) were used throughout the experimental work. Multi component tablet thiofenac-*o* 4 mg (TCH 4 mg and DIC 50 mg) was procured from local market.

Standard stock solution: Standard stock solutions of TCH and DIC were prepared in double distilled water in a concentration of 100 µg/mL of TCH and DIC respectively. Aliquot portions of stock solutions were diluted with double distilled water to get final concentration of 10 µg/mL each. The final diluted solution was scanned within the range of 400-200 nm in 1 cm cell against blank separately to get the absorbance graph for both the drugs and the overlain spectra.

Determination of absorptivity value: The solutions of each drug in triplicate were read against solvent blank at the selected wavelengths and absorptivity (A) (1 % 1 cm) value were calculated using the formula:

$$\text{Absorptivity A}(1\%1\text{cm}) = \frac{\text{Absorbance}}{\text{Concentration in g}/100\,\text{mL}}$$

Study of linearity: Stock solutions each of TCH and DIC having concentration of 100 µg/mL were prepared. Aliquots of each solution were appropriately diluted and the final dilutions were read at the selected wavelengths individually and in their combination. The correlation coefficient was found to be less than 1. The method was first applied to the standard laboratory mixture, which yielded encouraging results and the proposed methods were applied to the marketed formulation.

Assay of formulation: Twenty tablets were weighed and average weight was calculated. The tablets were triturated thoroughly and mixed. Tablet powder equivalent to 4 mg of thiocolchicoside (*ca.* 50 mg of diclofenac potassium, on the basis of label claim) was transferred to 50 mL with sufficient quantity of distilled water and volume was made up to the mark with distilled water. The content was filtered through Whatman filter paper (no. 41). A 5 mL portion of the above filtrate was further diluted to 50 mL with distilled water. The final dilution of all sample solutions were recorded at the selected wavelengths using distilled water as a blank solution. The amount of each drug was estimated by proposed methods using the following formula[11]:

Simultaneous equation method (method A): The absorbance and the absorptivity values at these particular wavelengths were calculated and substituted in the following equation, to obtain respective concentration:

$$C_{TCH} = A_1ax_2 - A_2ax_1 / ax_2ay_1 - ax_1ay_2 \quad (1)$$

$$C_{DIC} = A_1ax_2 - A_2ax_1 / ax_2ay_1 - ax_1ay_2 \quad (2)$$

A_1 and A_2 are absorbance of diluted laboratory mixture at 260 and 277 nm, respectively. Cx and Cy are concentrations of TCH and DIC respectively (g/100 mL). ax_1 and ax_2 are absorptivities of TCH and DIC at 260 nm while ay_1 and ay_2 are absorptivities of TCH and DIC at 277 nm, respectively.

Absorbance ratio method (method B):

$$C_{TCH} = Qm - Qy.A_1 /Qx - Qy.ax_1 \quad (3)$$

$$C_{DIC} = Qm - Qy.A_2 /Qx - Qy.ay_2 \quad (4)$$

where, Qm = absorbance ratio of sample mixture at 260/266 nm; Qx = ratio of absorptivity of DIC at 260/266 nm; Qy = ratio of absorptivity of TCH at 260/266 nm; ax_1 = absorptivity of TCH at 260; ay_1 = absorptivity of DIC at 266; A = absorbance of sample mixture at isobestic wavelength (266 nm).

Amount of drugs are calculated by using following formula:

of Drug (mg) = conc. of drug (mg) × dilution factor

The percentage estimation of each drug was calculated by using the following formula:

$$\text{Estimation (\%)} = \frac{\text{Amt.estimated (mg)}}{\text{Amt. taken (mg)}} \times 100 \quad (5)$$

Method validation: Validation of the proposed methods were carried out for its accuracy, precision, specificity and ruggedness according to ICH guidelines[12].

Accuracy: Recovery studies were carried out at four different levels by adding the pure drug to previously analyzed tablet powder sample. From the amount of drug total drug found, percentage recovery was calculated by proposed three methods.

Precision

Inter-day precision: It was done by analyzing the solutions by same analyst on alternate days till 5th day.

Intra-day precision: It was done by analyzing the solutions by same analyst within a day.

Specificity: Accurately weighed quantities of tablet powder equivalent to about 2 mg TCH, were transferred to 50 mL volumetric flask. All samples were stored for 24 h under following different conditions.

(a) At 50 ºC after addition of 1 mL of 1 % CH_3COOH (acid); (b) At 50 ºC after addition of 1 mL of 1 % NaOH (alkali); (c) At 50 ºC after addition of 1 mL of 1 % H_2O_2 (oxide); (d) At 60 ºC (heat).

After 24 h sufficient quantity of water was added and shaked for 0.5 h. And further the volume was made up to the mark. The content of the flask were filtered through Whatmann filter paper (no. 41). 5 mL portions of the filtrate were further diluted with distilled water to 50 mL. The final dilutions of sample solutions were then scanned over a range of 260 to 277 nm in multicomponent mode against solvent using distilled water as a blank. The content of each drugs and % label claim was calculated using the same formula as described in marketed formulation assay.

Linearity and range: Accurately weighed quantities of tablet content equivalent to about 80, 90, 100, 110 and 120 % of label claimed of TCH were taken and dilutions were made as described under marketed formulation. The sample solutions were scanned over a range of 400 to 200 nm in multicomponent mode against solvent using distilled water. The content of each drug was calculated using the same formula as described in marketed formulation.

RESULTS AND DISCUSSION

Both the methods were found to be simple, accurate, economic and rapid for routine simultaneous estimation of TCH and DIC in capsule dosage form. For two methods linearity was observed in the concentration range of 1-5 µg/mL for TCH and 12.5- 62.5 µg/mL for DIC (Table-1). Marketed brand of capsule was analyzed and amount of drug determined by proposed methods ranges from 100.68 to 100.94 %. The proposed methods were validated as per ICH guideline. The percentage recovery ranges from 98.75 to 101.0 % for both the methods (Table-2). Intermediate precision was calculated as was inter-day and intraday variations for both drugs. The results of both parameters indicate that the drug solution was found to be stable for a period of 1 h after the preparation of solution and thereafter the percentage label claim of TCH changes, indicates the drug undergoes some sort of degradation (Table-3). Further DIC was found to be stable for period of 5 days and there after the percentage label claim differs from normal. Hence it could be suggested that the stability of drug in solution remains for 1 h (Table-4). The results obtained by **method A** and **B** for the estimation of thiocolchicoside and diclofenac potassium were studied statistically by unpaired T-test with Welch correction. The result of analysis of marketed formulations by proposed methods which are within statistical limits.

TABLE-1
RESULTS OF ESTIMATION IN MARKETED FORMULATION

Weight (mg)	Amt. estimated in avg. wt. of tablet (mg)				Label claim (%)			
	Method (A)		Method (B)		Method (A)		Method (B)	
	TCH	DIC	TCH	DIC	TCH	DIC	TCH	DIC
225	2	25	2.1	25	101.2	100.4	101.2	100.1
225.2	2.2	25.2	2.3	25.2	101.6	101.2	102.1	101.3
224.9	2	24.9	2.1	24.9	101.2	99.8	101.7	99.8
224.8	2	24.8	2.1	24.8	99.8	102	100	101.9
225.1	2.1	25.1	2.2	25.04	100.9	100	101.6	100.2
Mean					100.94	100.68	101.32	100.66
± SD					0.68	0.91	0.84	0.84
% RSD					0.67	0.90	0.83	0.83

TABLE-2
RESULTS OF RECOVERY STUDIES

Pure drug added (mg)		Amount of pure drug recovered (mg)				Recovery (%)			
		Method A		Method B		Method A		Method B	
TCH	DIC	TCH	DIC	TCH	DIC	TCH	DIC	TCH	DIC
2	25	2.04	25.78	2.12	25.75	100.7	100.2	103	99.7
1.9	24.9	1.99	25.12	2.08	25.15	102.0	98.9	102	98.7
1.9	24.9	2.05	25.41	2.75	25.36	101.3	99.2	101.3	98.5
2	25	2.45	25.62	2.5	25.48	99.5	99.3	100	98.1
Mean						100.8	99.4	99.4	99.4
± SD						1.06	0.56	1.26	0.68
% RSD						1.05	0.55	1.25	0.67

TABLE-3
RESULTS OF RUGGEDNESS STUDIES

Parameter	Mean percent of label claim ± RSD (%)			
	Method (A)		Method (B)	
	TCH	DIC	TCH	DIC
Precision intra-day (n-5)	100.94 ± 0.61	100.68 ± 0.82	101.32 ± 0.72	100.66 ± 0.80
Precision interday (n-5)	100.87 ± 0.92	99.4 ± 0.48	101.57 ± 1.09	98.75 ± 0.59

TABLE-4
RESULTS OF ESTIMATION STABILITY STUDIES

Condition	Wt taken (mg)	Amt. Estimated in avg. wt of tablet (mg)				Label claim (%)			
		Method (A)		Method (B)		Method (A)		Method (B)	
		TCH	DIC	TCH	DIC	TCH	DIC	TCH	DIC
Normal	224.9	1.9	24.9	2.0	25.0	105.2	100.4	100.0	100.0
1 % CH_3COOH	225.0	2.0	25.0	2.1	25.1	100.0	100.0	**95.2**	99.6
1 % NaOH	225.0	2.0	25.0	2.1	25.1	100.0	100.0	**95.2**	99.6
1 % H_2O_2	224.9	1.9	24.9	1.9	24.9	**105.9**	100.4	**105.2**	100.4
60 ºC	224.9	1.9	24.9	2.0	25.0	**105.9**	100.4	100.0	100.0

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REFERENCES

1. The Merck Index, An Encyclopedia of Chemicals, Drugs and Biological, Merk & Co., Inc., NJ, edn. 13, p. 9397 (2001).
2. Q. Lu, C.L. Copper and G.E. Collins, *Anal. Chim. Acta*, **572**, 205 (2006).
3. N.A. El-Ragehy, M.M. Ellaithy and M.A. El-Ghobashy, *IL Farmaco*, **58**, 463 (2003).
4. A. Rosso and S. Zuccaro, *J. Chromatogr. A*, **825**, 96 (1998).
5. G. Forni and G. Massarani, *J. Chromatogr. A*, **131**, 444 (1977).
6. British Pharmacopoeia, 2, Controller of Her Majesty's Stationary Office, Norwish (2007).
7. J.A. Arancibia, M.A. Boldrini and G.M. Escandrav, *Talanta*, **2**, 261 (2000).
8. W. Thongchai, B. Liawraungrath, C. Thongpoon and T. Machan, *Chiang Mai J. Sci.*, **33**, 123 (2006).
9. C. Arcelloni, R. Lanzi, S. Pedercini, G. Molteni, I. Fermo, R. Paroni and A. Pontiroli, *J. Chromatogr. Biomed. Sci. Appl.*,**763**, 195 (2001).
10. S.V. Mulgund, M.S. Phoujdar, S.V. Londhe, P.S. Mallade, T.S. Kulkarni and A.S. Deshpande, *Ind. J. Pharm. Sci.*, **71**, 35 (2009).
11. A.G. Davidson, A.H. Beckett and J.B. Stenlake, Practical Pharmaceutical Chemistry, CBS Publishers & Distributor, New Delhi (2001).
12. Internatinal Conference on Hormonization, ICH Harmonized Tripartite Guidelines-Validation of Analytical Procedures, Federal Register, p. 27463 (1997).