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Simultaneous determination of paracetamol and ibuprofen from combined dosage formulation by HPTLC method

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ABSTRACT

In the present communication simultaneous determination of paracetamol and ibuprofen from pharmaceutical preparation by high performance thin layer chromatographic is described. The assay was carried out by using CAMAG Linomat IV applicator in precoated HPTLC plate with silica gel 60F, 20 x10 cm, Merck no. 5642. Ethyl acetate: acetone: butanol : ammonia in the ratio of 30: 40: 30: 10 (v/v) was constituted as solvent system. Diloxanide furoate was used as internal standard. The evaluation was performed at 254 nm. The R_f values of paracetamol and ibuprofen were 0.86 and 0.32 respectively. The calibration curves were found to be linear in the concentration range of 1.2- 6.0 and 1.3-6.5 µg/ ml for paracetamol and ibuprofen respectively. The results of the analytical methods were validated statistically. The proposed method can be successfully used to determine the drug contents in combined formulation.

KEYWORDS

Paracetamol;
Ibuprofen;
Diloxanide furoate;
HPTLC;
Pharmaceutical dosage form.

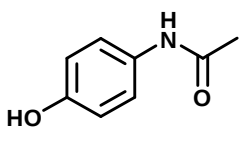
INTRODUCTION

Paracetamol is chemically described as N-(4-hydroxyphenyl)acetamide. It is analgesic, anti-inflammatory and antipyretic drug. Paracetamol is officially reported in BP[1], IP[2] and USP[3]. BP[1] and IP[2] suggests titrimetric and UV spectrophotometric methods for assay of paracetamol in bulk and tablet formulation respectively. USP[3] describes thin layer chromatographic method for determination of paracetamol.

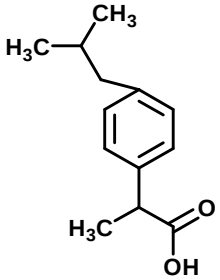
Ibuprofen is α –methyl -4-(2- methyl propyl) benzene acetic acid. It is widely used as anti-inflammatory drug. BP[1] and USP[3] suggest liquid chromatographic method for assay of ibuprofen in bulk and tablet formulation respectively. IP[2] describes chloroform extraction followed acid-base titration method for determination ibuprofen from tablet formulation.

The literature survey reveals that titrimetric[4], HPLC[5] and HPTLC[6] methods for simultaneous determination of paracetamol and ibuprofen from combined dosage form.

In this communication a new simple, rapid and reliable HPTLC method is reported for simultaneous de-



Structure of paracetamol



Structure of ibuprofen

termination of paracetamol and ibuprofen in combined dosage form by using internal standard. This method can be used for the routine analysis of such combination formulation in quality control laboratories. In the proposed work, optimization and validation of this method are reported.

EXPERIMENTAL

Materials

Reference standards of paracetamol and ibuprofen were obtained from reputed firms with certificate of analysis. Ethyl acetate, acetone, butanol, ammonia were used of AR grade and spectroscopic grade methanol was used.

Instrumentation

Camag Linomat IV as sample applicator, Camag TLC scanner II, Camag Twin tough chamber were used.

HPTLC pre-coated plates with silica gel 60F (20 x10 cm) Merck 5642 were used.

Sample volume: 15 µl.

Evaluation was carried at 254 nm.

Preparation of standard and internal standard solution

Standard solution of paracetamol was prepared by dissolving 60 mg of pure paracetamol in 50 ml of methanol. Standard solution of ibuprofen was prepared by dissolving 65 mg of pure ibuprofen in 50 ml of methanol. For working standard one ml of these solutions were diluted to 1000 ml with methanol. Internal standard solution of diloxanide furoate was prepared by dissolving 40 mg of pure diloxanide furoate in 50 ml of methanol. The working internal standard solution was prepared by diluting 10 ml of internal standard solution to 100 ml with methanol.

For mobile phase ethyl acetate: acetone: butanol: 10% ammonia were mixed in the ratio of 30: 40: 30: 10 (v/v).

Preparation of sample solution

Twenty tablets of the formulation under study were accurately weighed and weight of each tablet was determined. The powder equivalent to 60 mg of paracetamol and 65 mg of ibuprofen was weighed accurately. It was transferred in 50 ml of volumetric flask with 30 ml of methanol. Solution was sonicated for five minutes. The volume was adjusted to 50 ml with methanol. Sample solution was filtered through filter paper no.41. One ml of this solution was diluted to 1000 ml with methanol. This solution was used as working standard for analysis of formulation.

The 15 µl of this solution was spotted on a chromatographic plate with help of Linomat IV spotting system. After development of chromatograph plates, the bands of the drugs and internal standard were scanned at 254 nm and chromatograms were recorded. (Figure 4) On applying the appropriate dilution factor and by comparing the peak area ratios of the standards and the sample solutions, the amount of paracetamol and ibuprofen present per tablet was calculated.

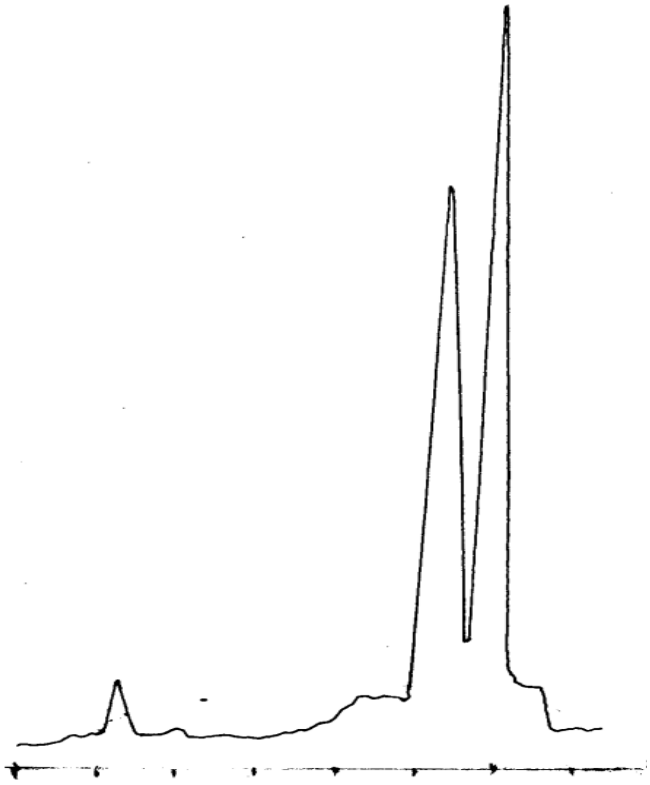


Figure 4 : Chromatograms of paracetamol and ibuprofen (From tablet)

Chromatographic conditions

Chromatographic separation was performed on chromatoplates of silica gel 60 F (20 x 10 cm) merck no 5642. Solvent system consists of ethyl acetate: acetone: butanol: 10 % (v/v) ammonia in a ratio of

30:40:30: 10 (v/v). The sample volume was used for analysis as 15 µl.

Method development

Into series of 10 ml of standard volumetric flasks varying aliquots of the working standard solution of paracetamol drug solution were taken. To each flask 1 ml of working internal standard solution was added. The contents were diluted up to mark with methanol and were mixed thoroughly.

The 15 µl of the solution was spotted on a chromatoplate with help of Linomat IV spotting system. The twin trough chamber was allowed to saturate with the mobile phase vapour for ten minutes. The plate was developed in mobile phase and allowed to travel a distance of 76 mm above the position of sample application. The UV response of the well resolved bands of the drugs and internal standard was monitored using scanning densitometer set at 254 nm. The chromatogram was recorded. A typical chromatogram was given in figure 1 and peak areas were given in TABLE 1. R_f values are given in TABLE 2. A plot of peak area ratios of the drug in the internal standard against concentration of the drug in µg was found to be linear in the concentration range of 1.2 to 6.0 µg / ml.

TABLE 1 : Peak areas of paracetamol and ibuprofen

No.	Concentration of paracetamol in µg/ ml	Concentration of ibuprofen in µg/ ml	Peak area of paracetamol	Peak area of ibuprofen
1.	1.2	1.3	0.766	0.05555
2.	2.4	2.6	1.532	0.11110
3.	3.6	3.9	2.296	0.1660
4.	4.8	5.2	3.065	0.2220
5.	6.0	6.5	3.830	0.2770

TABLE 2 : R_f values of paracetamol, ibuprofen and diloxanide furoate

Sr. No.	Name of the drug	Distance traveled in mm	R_f value
1.	Solvent	76	-
2.	Diloxanide furoate	71.5	0.94
3.	Paracetamol	65.5	0.86
4.	Ibuprofen	24.5	0.32

Similar procedures were performed for standard solution of ibuprofen. Typical chromatogram is given in figure 2.

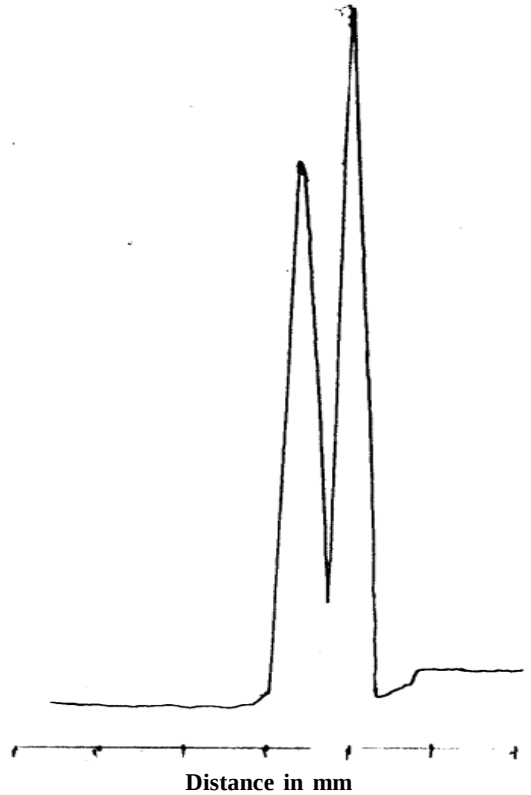


Figure 1 : Chromatogram of paracetamol (standard)

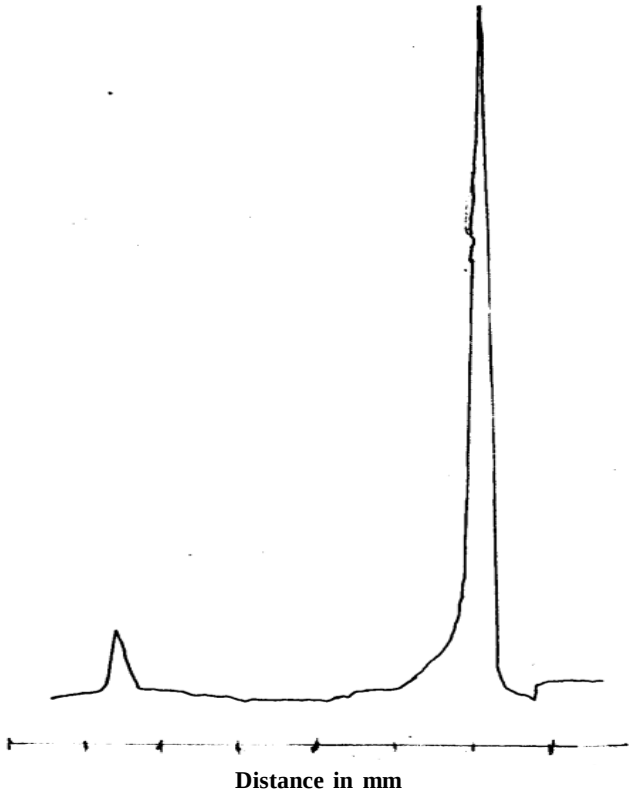


Figure 2 : Chromatogram of ibuprofen (standard)

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Into series of 10 ml of standard volumetric flasks varying aliquots of the working standard solution of paracetamol and ibuprofen drug solutions were taken. To each flask 1 ml of working internal standard solution was added. The contents were diluted up to mark with methanol and were mixed thoroughly. Similar procedures were performed. Typical chromatogram was recorded. It is given in figure 3.

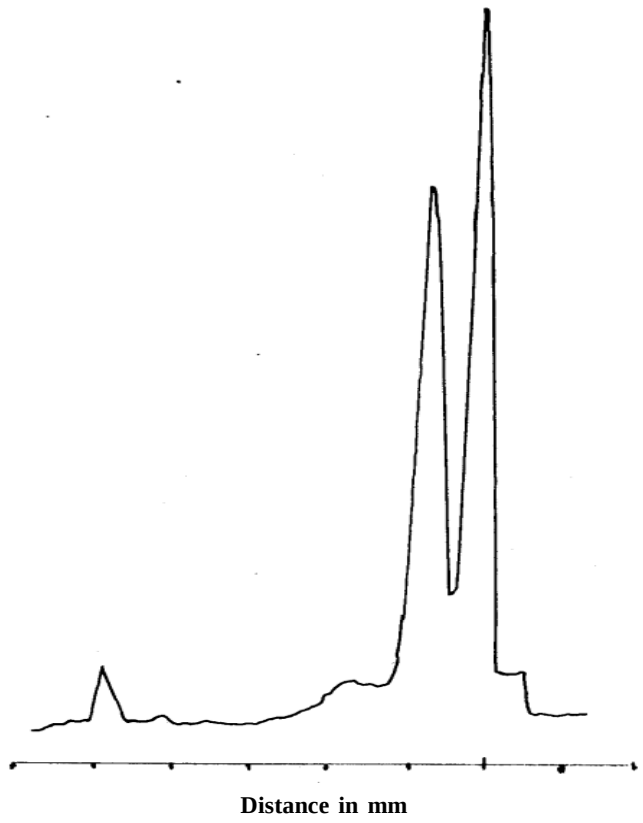

Figure 3 : Chromatograms of paracetamol and ibuprofen (standard)

RESULTS AND DISCUSSION

System suitability

System suitability parameters of the developed HPTLC method were determined by spotting standard solutions. Experimental factor such as R_f value was determined. The results are given in TABLE 2.

Linearity

Under the experimental conditions described above, linear calibration curves for all the two drugs were obtained throughout the concentration ranges studied. Regression analysis was done on the peak areas of the two drugs i.e. (y) v/s concentration (x). The regression analysis data obtained is tabulated in TABLE 3. The linear ranges were 1.2- 6.0 µg/ ml of paracetamol, and 1.3 – 6.5 µg/ ml of ibuprofen.

TABLE 3 : Linearity-regression analysis data

Parameters	Paracetamol	Ibuprofen
Correlation coefficient	0.9917	0.9999
Intercept (c)	0.0677	0.00005
Slope (m)	0.6330	0.0427

Accuracy

Accuracy of the proposed method was determined by applying the described method to synthetic mixture containing known amount of each drug corresponding to 80 %, 90% and 100 % of the label claim. The accuracy was then calculated as the percentage of analyte recovered by the assay. The results of the recovery analysis are enclosed under TABLE 4.

TABLE 4 : Accuracy – Percent recovery of each analyte

Drug	Amount of Drug taken in mg.	Amount of drug added in mg.	Total amount drug found in mg.	Percentage error (%)	% recovery	% RSD
Paracetamol	150	0	-	-	-	-
	150	120	119.82	0.15	99.85	0.2773
	150	135	134.96	0.03	99.97	0.2241
	150	150	150.39	0.026	100.026	0.1057
Ibuprofen	162.5	0	-	-	-	
	162.5	130	129.93	0.0538	99.946	0.3082
	162.5	146.3	146.17	0.0846	99.91	0.17046
	162.5	162.5	162.51	0.01	100.01	0.06987

Precision

The method Precision was established by carrying out the analysis of powder blend containing two drugs. The assay was carried out of all the two drugs using

TABLE 5 : Precision-method precision

Experiment No.	Sample weight taken	content in mg/ tablet obtained of	
		Paracetamol	Ibuprofen
1.	167.4	298.75	325.00
2.	166.0	297.15	322.95
3.	166.4	297.73	323.62
4.	167.8	302.026	325.23
5.	166.8	298.12	323.97
6.	166.0	297.15	322.94

proposed analytical method in six replicates. The value of relative standard deviation lie well within the limits (0.1057- 0.2773 % for paracetamol and 0.06987-0.3082 % for ibuprofen), indicated the sample repeatability of the method. The results obtained are tabulated in TABLE 5.

Stability of solution

Stock solution stability was checked for 24 hrs at room temperature. The drug solutions were found to be stable for the specified period. Stock Solution of sample and standard contain 120 µg/ ml of paracetamol and 130 µg/ ml ibuprofen.

Method application

The validated HPTLC method was applied to simultaneous determination of paracetamol and ibuprofen. Twenty tablets mixture contains paracetamol (300 mg) and ibuprofen (325 mg) were used. A portion equivalent to 60 mg of paracetamol and 65 mg of ibuprofen was weighed accurately. It was dissolved in 30 ml of methanol. It was mixed well and further diluted to get a solution of concentration of 120 µg /ml paracetamol and 130 µg /ml of ibuprofen. One ml of this solution is diluted to 1000 ml. A 15 µl of this solution was spotted on chromatographic plate. The analyte peaks were identified by comparison with observed retention times with those of respective standard. The peak areas obtained were used to calculate the drug present. The assay results are expressed as mg /tablets in TABLE 5.

CONCLUSION

The proposed method is first HPTLC method by using internal standard method for determination paracetamol and ibuprofen in combined dosage form. The proposed HPTLC method provides a fast, accurate and rugged assay with stability for these two drugs in mixture formulation or in solution alone.

The proposed methods two drugs gave well defined peaks. They were well separated. The reproducibility, repeatability and accuracy of the proposed method were found to be satisfactory which is evidenced by low values of standard deviation and percentage relative standard deviation in comparison to previous methods. The accuracy and reproducibility of the proposed method was confirmed by recovery experiments, performed by adding known amount of the drugs to pre analyzed formulation and reanalyzing the mixture by the proposed method. The percentage recovery obtained indicates non-interference from the excipients used in the formulation.

In this method internal standard is used. In the previous method internal standard was not used. Thus the proposed HPTLC method for the simultaneous determination of paracetamol and ibuprofen in combined dosage formulation is precise and accurate. It is applicable at very low concentration as compared to previous method suggested in literature[6]. Hence the proposed HPTLC method is strongly recommended for the quality control of raw material, formulation.

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REFERENCES

[1] 'British Pharmacopoeia', Her Majesty's Stationary Office, London, **1-3**, **(2008)**.

[2] 'Indian Pharmacopoeia', Controller of Publication, Delhi, **1-3**, **(2007)**.

[3] 'United States Pharmacopoeia', US Pharmaceutical Convention Inc., Rockville, Washington DC, USP 31 NF 26, **1-3**, **(2008)**.

[4] P.Parimoo, R.R.Sethuraman, A.Amalraj, N.Seshadri; Indian Drug, **26(12)**, 704-705 **(1989)**.

[5] R.Jain, C.L.Jain, Y.K.Bansal; Indian Drug, **27(12)**, 615-617 **(1990)**.

[6] P.P.Shirke, M.K.Patel, V.A.Tamahane, V.B.Tirodkar, P.D.Sethi; Indian Drug, **30(12)**, 653-654 **(1993)**.