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Development of a Method for Determination of Diphenhydramine HCl and Ibuprofen in Pharmaceutical Preparations (Tablets)

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ABSTRACT

Purpose: To development a new high-pressure liquid chromatography (HPLC) technique for determination analysis of diphenhydramine hydrochloride (DPH) and ibuprofen (IBU) in tablet.

Methods: Chromatographic conditions were an isocratic system with C18-column (250 mm x 4.6mm,5µm), flow rate 1.0 ml/min and detector UV at 254 nm, And a mixture of 0.05 M of KH_2PO_4 buffer and acetonitrile (50:50) and this mixture, acetonitrile -triethylamine (70:30:0.3), v/v, pH 3,0) as mobile phase. The method was validated for selectivity, linearity, detection limit, LOQ, precision, and accuracy.

Results: Retention time of DPH and IBU were 4.3, 15.6 min, respectively. The method showed good selectivity, calibration curves were linear over the concentration range of 10– 100 µg/mL for DH, with correlation coefficient of 0.9997, and 50– 500µg/mL for IB, with correlation coefficient of 0.9996 accuracy was 99.46 - 100.20 and 100.01- 101.05 % DPH and IBU, respectively; precision (RSD) was < 1.0.

Conclusion: This method is sensitive, precise, highly selective, and accurate, and would be suitable for the simultaneous analysis of DPH and IBU in tablet dosage form. Since methanol is cheaper than acetonitrile, the application of the method may reduce the cost of analysis.

Keywords: Diphenhydramine HCl, Ibuprofen, Tablet

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INTRODUCTION

High-performance liquid chromatography (HPLC) is a separation technique that can be used for the analysis of organic molecules and ions. HPLC is based on mechanisms of adsorption, partition and ion exchange, depending on the type of stationary phase used. HPLC involves a solid stationary phase, normally packed inside a stainless-steel column, and a liquid mobile phase. Separation of the components of a solution results from the difference in the relative distribution ratios of the solutes between the two phases[1].Mobile phase, flow rate and detector play an important role in separation and detection of analyte in matrix of sample [4-6].

The direct determination of drugs by HPLC depend upon the physical properties of drngs [7- 9] while the indirect determination of drugs depend upon the chemical properties of drug with metal to form metallo - drug [10], or oxidative coupling of drug with other reagent in presence of acid or alkaline media [11]. There are three properties such as peak height, peak area and internal standard and used for determination of drug by HPLC. HPLC is accomplished by injection of a small amount of liquid sample into a moving stream of liquid (called the mobile phase) that passes through a column packed with particles of stationary phase. Separation of a mixture into its components depends on different degrees of retention of each component in the column. The extent to which a component is retained in the column is determined by its partitioning between the liquid mobile phase and the stationary phase. In HPLC this partitioning is affected by the relative solute/stationary phase and solute/mobile phase interactions [12,13].

EXPRIMENTAL WORK

preparation solution

Standard solutions

Stock solutions were prepared by dissolving 50 mg of IBU and 10 mg of DPH in 100 ml volumetric flask and diluents. And these solutions were prepared by diluent the stock solutions with the mobile phase two of 500 ppm (IBU) and 100 ppm (DPH), were filtered through 0.20 micrometer filter before starting the testes.

Mobile Phase

Mobile phase was prepared by dissolving of 0.05 M of KH_2PO_4 buffer and acetonitrile (50:50) and this mixture, acetonitrile -triethylamine (70:30:0.3), v/v, pH 3,0).

Sample preparation

Ten tablets were weighed and grinded with mortar, an amount of the tablets powder equivalent to 50 µg.ml^{-1} of IBU and 10 µg.ml^{-1} of DPH. and the mixture was filter and heating and ultra-sonication for 30 min and filtered through 0.48 micrometer. The linear calibration curves were obtained over the concentration ranges of 50 to 500 ppm for IBU and 10 to 100 ppm for DPH.

Table 1. The best conditions for determination drug

Analytical parameters	DPH - IBU
Mobile phase	mixture of 0.05 M of KH_2PO_4 buffer and acetonitrile (50:50) and this mixture, acetonitrile -triethylamine (70:30:0.3), v/v, pH 3,0)
Stationary phase =	C18- column (250 mm x 4.6mm,5µm)
Linear range µg /ml	10– 100 for DH, and 50– 500 for IB
Recovery	99.46 - 100.20 % DPH and 100.01- 101.05 % IBU
Correlation coffient	0.9986
λmax nm	254 nm
Detection limit µg /ml	2.8×10^{-5}
Standar deviation	0.054
Flow rate ml / min	1.0
pH	4.5
Pharmaceutical formulation	Tablet
Type of HPLC	RP - HPLC
Cegression line	Y = 4976 X + 6384
Retention time (min)	4.3 DPH -15.7 IBU

Table 2. The best analytical Parameters for determination drug

Drug	SP	PE (mv)	PH (mv)	RT (mint)	N	HETP	Rec. %
DPH - IBU	C_{18}	1601633 13017275	100872 345239	4.391 15.739	1545.4	0.1423	99.46 100.01

SP = Stationany phase

pH = Peak height; MV = millivolt; RT = retention time; N = Number of theoretical plates; HETP = High Equivalent theoretical plates

Selection of Column

The best separation column is selected for the DIH drug of type C_{18} (250mm × 4.6mm × 5µm) due to its high separation efficiency.

Effect of column on separating of drug

20 µl of DPH solution of 10 ppm concentration are injected separately in three columns C-No_2, carbon atom $_{18}$, carbon – silica, in HPLC apparatus and the response is recorded for each column. The outcome is shown in Table 3 and Figure (1). And the results are choosing the column carbon atom $_{-18,}$ for an important reason there is the retention time is little and the peak is sharp. The measurements are a responses of peak areas compared with the responses of peak areas of the C.R.S. (Chemical reference standard). The column C_{-18} is chosen as the best column because of a low value of HETP and good number of theoretical plates (N).

The selected mobile phase

The mobile phase ratio is effected on the chromatogram and the dwell time is studied by taking a different proportions of the mobile phase of dissolve mixture of 0.05 M of KH_2PO_4 buffer and acetonitrile (50:50) and this mixture, acetonitrile -triethylamine (70:30:0.3), v/v, pH 3,0). becuse the appearance of strong and obvious peak, small retention time.

The effect of wavelength (λ max)

20µl of standard DPH and IBU solution are injected and the response (peak area) is recorded at (two hundred and forty, two hundred and fifty-four, two hundred and sixty) nm. It is the better curve is at two hundred and fifty-four nm where a sharp tip and little retention time are obtained. This wavelength is therefore adopted in the next experiments.

Selection of Flow rate for mobile phase

20µl aliquot of 10 ppm solution from DIH and IBU is injected and the (m.ph) with (F.R) between (0.8 – 2.0) ml.minute^{-1} at 254 nm are used. At the flow rate of indicating to good separation efficiency (1.0) ml. minute^{-1} at appearing the sharp peak, a small retention time. The flow rate of 1.0 ml.min^{-1} is choose because of the small HETP and high number of plates.

Preparation Calibration Curve for the drug

In a series of 10ml volumetric flasks, concentrations ranged IBU (10-50 part per million) and concentrations ranged DPH (5-25 part per million). and complete the volume up to the mark with the (m.ph). 20 µl of each concentration is injected in stationary phase carbon atom $_{-18}$, and using the (m.ph) mixture of 0.05 Molarity of KH_2PO_4 buffer and acetonitrile (50:50) and this mixture, acetonitrile -triethylamine (70:30:0.3), v/v, pH 3,0) and (F.R) 1.0 ml / minute· the response was recorded (peak height) at 254 nm. The values are shown in table (three, four) and the Figure (one, two).

Table 3. Peak height and statistical information of the calibration curve IBU

NO.1	Conc. (ppm)	Peak height (mv)	Conc.found (µg.ml ^{1})	RSD	R.E %	Recovery %	Standard deviation
1	10	345239	10.4255	0.0006	0.0425	104.255	238.7065
2	20	363543	19.2458	0.0003	-0.0377	96.229	129.4230
3	30	385976	30.0559	0.0005	0.0018	100.186	215.8386
4	40	407543	40.4486	0.0003	0.0112	101.121	147.1149
5	50	426999	49.8241	0.0004	-0.0035	99.648	179.3544

Table 4. Peak height and statistical information of the calibration curve DPH

NO.1	Conc. (ppm)	Peak height (mv)	Conc.found (µg.ml ^{1})	RSD	R.E %	Recovery %	Standard deviation
1	5	100872	5.1978	0.0020	0.0395	103.9561	206.4045
2	10	115654	9.8910	0.0002	-0.0108	98.9109	26.1476
3	15	130543	14.6183	0.0008	-0.0254	97.4557	114.8020
4	20	148432	20.2981	0.0013	0.0149	101.4907	204.4473
5	25	163222	24.9939	0.0016	-0.0002	99.9758	276.1355

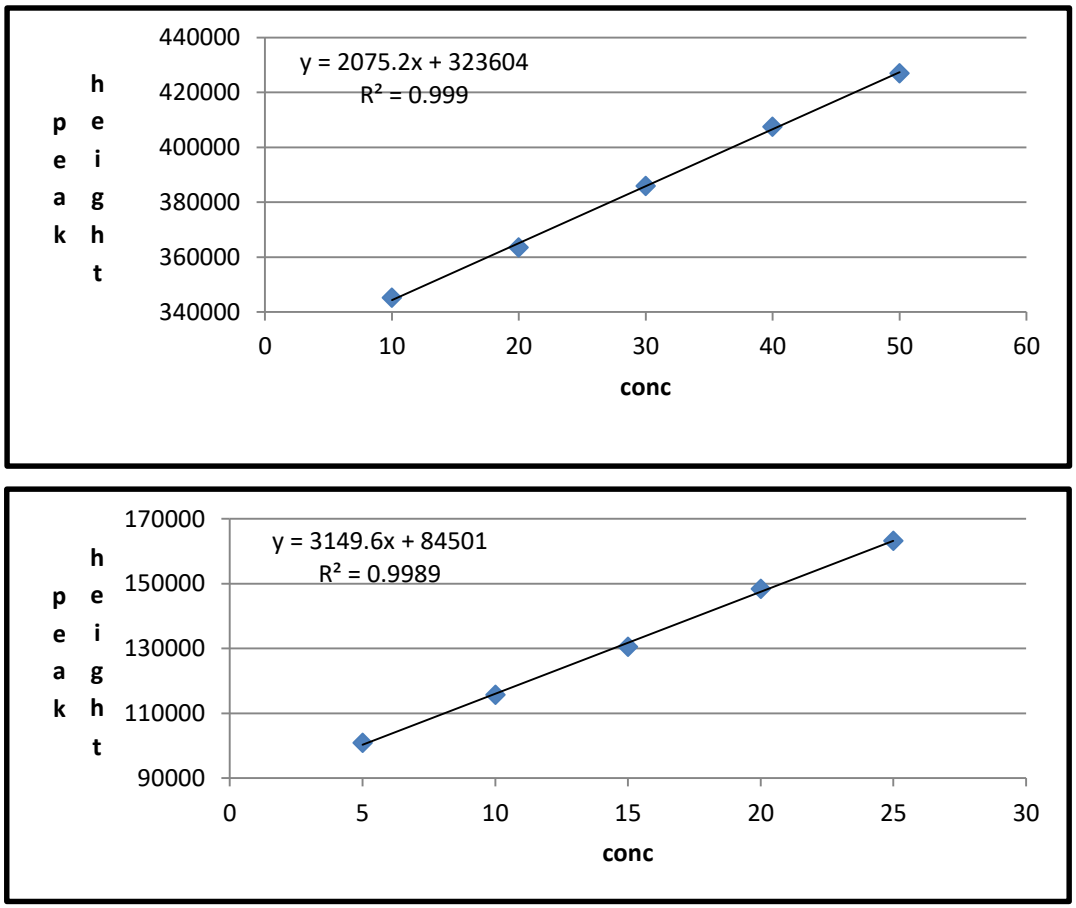

Figure 2. Calibration curve for the determination of DPH by a new developed method.

Evaluation of the results

The results are evaluated by using test T. and F. Value for comparison between these methods for determination of drug and standard methods used in British pharma Copeia B.P 2005. t - test for this experiment is less than tabular value at reliable level 95 %. F. Value for experiments is also less than turban value at reliable level 95 %

Simultaneous of (HPLC) determination of Advil PM in tablets 200mg IBU, 38mg DPH.

Weigh 10 tablets Advil PM, and this tablets is grinded with mortar 200mg IBU, 38mg DPH in 100ml of conical flask with

solvent consist of mixture of 0.05 M of KH_2PO_4 buffer and acetonitrile (50:50) and this mixture, acetonitrile - triethylamine (70:30:0.3), v/v, pH 3,0),and shacking 30 min. and ultrasonication and this solution is filtered in filter paper 0.48 µm. and complet the volume up to the mark with the same solvent. then pipett take 2.5ml of this solution and dilute to 25ml with the same solvent. using column type carbon atom-$_{18}$, and mobile phase consisting of mixture of 0.05 M of KH_2PO_4 buffer and acetonitrile (50:50) and this mixture, acetonitrile -triethylamine (70:30:0.3), v/v, pH 3,0) were used, and flow rate 1.0 ml/min. at 254nm.The result is compared with chemical reference standard C.R.S. with the same concentration. and the chromatogram is shown on the Table (5), Figure (3,4).

Table 5. Result of determination of Advil PM in drug preparation is product

Substance mg/tablet	Found mg/tablet	Peak height(mv)	Number of theoritical	HETP	Recovary %
Advil PM200ibu	199.2	50927	1476.6686	0.1693	99.6
Advil PM38dph	38.1	50927	1476.6686	0.1693	100.2

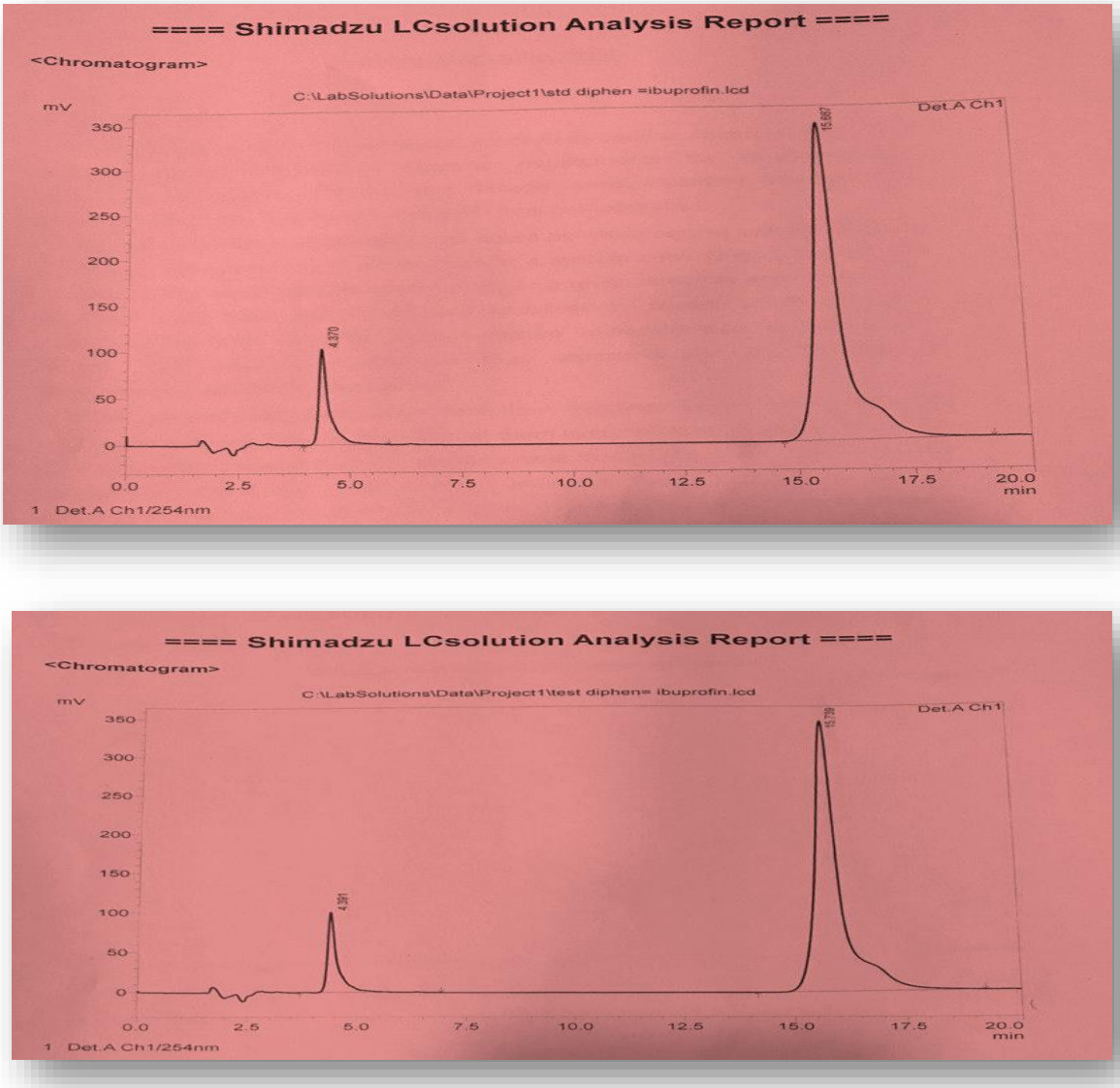

Figure 4. Chromatograms sample of dissolution,diphenhydramine HCl, ibuprofen.

DISCUSSION

The results in Tables (1) and (2) indicate that analytical method using in this research is accurate shish recovery and precise low standard deviation. The detection limit in this study was calculated and the results were taken as average of five readings it was observed that detection limit of DPH. The t - test and F - test for recent method is less than tabular valve at same reliable level as % indicating that no significant differences between standard method and proposed method. The best separation of drug must be gives good band, low HETP and high recovery. That fact agrees. The results indicate that no significance differences between original recovery be for addition and after addition of carbohydrate

solution this indicates that this indicates that the method is not suffering from interfaces effect, therefore this method is highly recommended for determination of drug by HPLC due to sensitively and decrease the retention time of drug leading to less using quantity of mobile phase, which is good in view of economic situation.

CONCLUSION

This method is sensitive, precise, highly selective, and accurate, and would be suitable for the simultaneous analysis of DPH and IBU in tablet dosage form. Since methanol is cheaper than acetonitrile, the application of the method may reduce the cost of analysis.

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