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DEVELOPMENT AND VALIDATION OF STABILITY-INDICATING HPTLC METHOD FOR SIMULTANEOUS ESTIMATION OF ENALAPRIL MALEATE, HYDROCHLOROTHIAZIDE AND PARACETAMOL IN COMBINED TABLET DOSAGE FORM

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ABSTRACT

A stability-indicating high-performance thin-layer chromatographic (HPTLC) method has been developed for the determination of simultaneous determination of Enalapril maleate (ENAL), Hydrochlorothiazide (HCTZ) and Paracetamol (PARA) in tablet dosage forms, The separation was achieved on TLC aluminum plates precoated with silica gel 60F-254 using chloroform: methanol: toluene : ethyl acetate (20:10:40:30 % v/v/v/v) as the mobile phase. The densitometric analysis was carried out at 230 nm. Compact bands appeared at R_f 0.21 ± 0.01, 0.50 ± 0.02 and 0.73 ± 0.01 respectively, for ENAL, HCTZ and PARA. Linear regression analysis revealed linearity in the range of 1000 – 6550 ng/spot for ENAL, 100-3600 ng/spot for HCTZ and 500 – 3400 ng/spot for PARA. Drugs were subjected to acid and alkali hydrolyses, forced oxidation, thermal and photo degradation treatments. The degraded products were well separated from the pure drugs. Statistical analysis proved that the method is precise, accurate, selective and economical and may be used for routine analysis of ENAL, HCTZ and PARA in tablet dosage forms.

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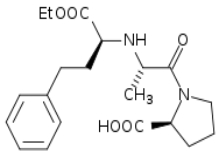
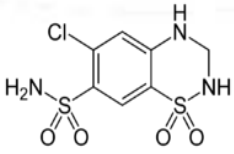
INTRODUCTION:

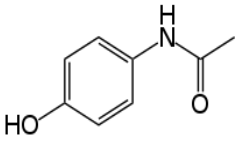
Enalapril Maleate is an angiotensin converting enzyme (ACE) inhibitor used in the treatment of hypertension and some types of chronic heart failure, hydrochlorthiazide, is a first line diuretic drug of the thiazide class that acts by inhibiting the kidneys' ability to retain water, paracetamol are widely used as an analgesic.[1-5]



Enalapril Maleate



Hydrochlorothiazide



Paracetamol

EXPERIMENTAL:

HPTLC method for simultaneous estimation of ENAL, HCTZ and PARA in combined tablet dosage form was developed using HPTLC (CAMAG (Muttenz, Switzerland). Chloroform: Methanol: Toluene: Ethyl acetate (20: 10: 40: 30 % v/v/v/v) was optimized as mobile phase.

Preparation of standard stock solution: Stock solution of each drug having concentration of 0.1 mg mL^{-1} (100 ng μL^{-1}) was prepared separately in mobile phase.

Analysis of commercial formulation: The method was applied for the quantitative study of drugs in commercially available tablets. For the preparation of the stock solution of tablet dosage form, 20 tablet of INVOZIDE (Ranbaxy Laboratories Ltd, Dewas) were taken and their average weight was determined. 20 tablets were crushed and weighed. Powder equivalent to 5 mg of ENAL in 10 mL volumetric flask and dissolved in 5 mL of mobile phase with vigorous shaking for 5 minutes. The supernatant liquid was transferred to 10 mL of volumetric flask through a whatman no. 41 filter

paper. Five replicates of sample solutions were prepared and applied. The concentrations of these drugs were extrapolated from their respective calibration curves by using the peak area of densitogram.

RESULTS AND DISCUSSION:

The HPTLC method was developed and validated according to ICH guidelines. [1] ENAL, HCTZ and PARA have shown good linear relationship for ENAL, HCTZ and PARA in the working concentration range (linearity range) of 1000 to 6550 ng per band, 100 to 3600 ng per band and 500 to 3400 ng per band, respectively. Precision of the method was determined in terms of intra-day and inter-day variation (% RSD). The accuracy of the proposed method was evaluated by percentage recovery of all three drugs. (Fig. 1 shows the peaks, overlays and of ENAL, HCTZ and PARA at 215 nm, 270 nm and 245 nm respectively).

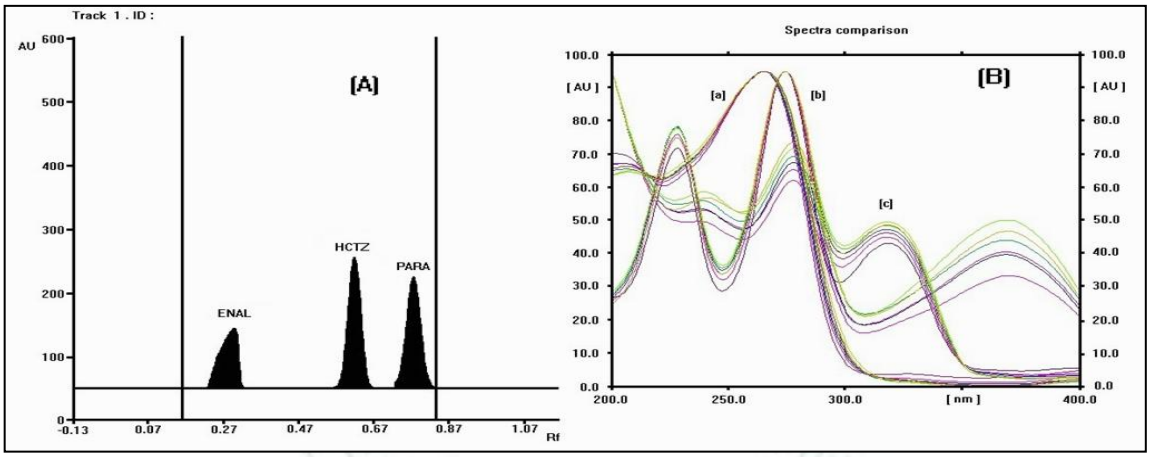


Figure 1: (a) Peaks (b) overlay of ENAL, HCTZ and PARA respectively

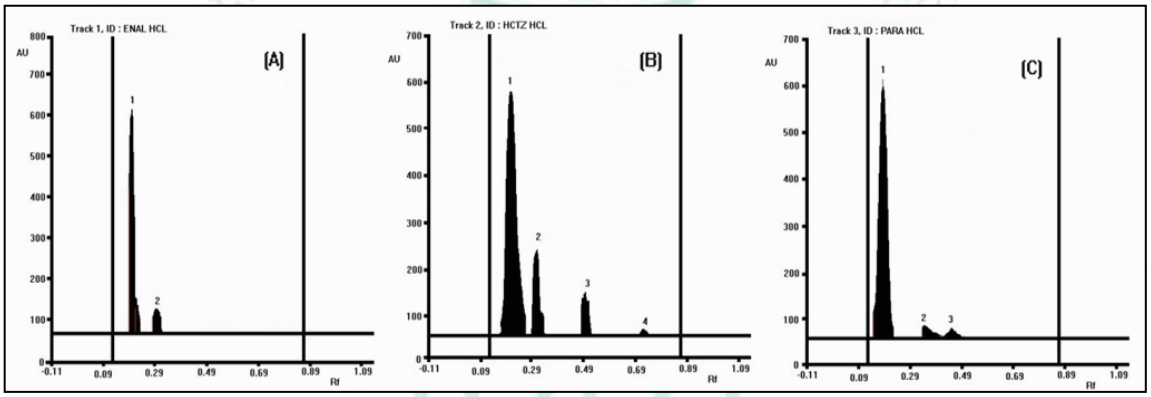


Figure 2: HPTLC chromatogram obtained from acid degradation for (a) ENAL (b) HCTZ (c) PARA

Table 1: Forced degradation study for ENAL, HCTZ and PARA

Parameters	Sample Exposure Condition	No. of Degradation Products (Rf Values)	% Recovery
ENAL	0.1 N HCl, 2 Hours, 60 ºC	1 (0.20)	61.52 ± 1.68
	0.01 N NaoH, 2 Hours, 60 ºC	3 (0.17, 0.33, 0.45)	69.28 ± 3.09
	13 % H_2O_2, 1 Hours, 60 ºC	3 (0.4, 0.78, 0.8)	81.69 ± 3.68
	Photo.chem, 8h	1 (0.32)	71.18 ± 2.70
	Dry Heat, 3h, 55 ºC	2 (0.34, 0.46)	73.35 ± 1.84
HCTZ	0.1 N HCl, 2 Hours, 60 ºC	3 (0.20, 0.42, 0.72)	81.11 ± 5.63
	0.01 N NaoH, 2 Hours, 60 ºC	3 (0.18, 0.45, 0.78)	63.87 ± 2.41
	13 % H_2O_2, 1 Hours, 60 ºC	4 (0.09, 0.15, 0.34, 0.71)	54.10 ± 3.26
	Photo.chem, 8h	2 (0.43, 0.72)	50.79±1.83
	Dry Heat, 3h, 55 ºC	3 (0.16, 0.23, 0.44)	61.42 ± 2.94
PARA	0.1 N HCl, 2 Hours, 60 ºC	2 (0.37, 0.39)	72.80 ± 2.93
	0.01 N NaoH, 2 Hours, 60 ºC	1(0.85)	76.82 ± 2.93
	13 % H_2O_2, 1 Hours, 60 ºC	1(0.89)	62.65 ± 2.14
	Photo.chem, 8h	1 (0.31)	50.76 ± 2.49
	Dry Heat, 3h, 55 ºC	2 (0.33, 0.74)	61.99 ± 2.08

Table 2: Validation parameters of the HPTLC method

Parameters		ENAL	HCTZ	PARA
Linearity range		1000-6550	500-3400	100-3600
Correl. coeff. (r^2)		0.993	0.996	0.995
Slope		2.8398	6.9042	5.079
Intercept		396.89	17.837	971.97
Recovery (%)		99.27 ± 0.41	99.85 ± 0.065	99.98 ± 0.023
Precision	Intraday (n = 3)	3255.1 ± 5.17	3505.33 ± 62.51	3274.86 ± 20.70
	Interday (n = 3)	3237.23 ± 71.47	3477.533 ± 21.0003	3284.367 ± 4.743
Repeatability		3345.65 ± 12.08	5429.967 ± 26.01	5077.4 ± 6.371
LOD		73.24	18.24	82.2
LOQ		221.9	55.3	249.1
Detection Wavelenth		215 nm	270 nm	245 nm
Rf Value		0.20 ± 0.04	0.55 ± 0.03	0.72 ± 0.02

Table 3: Summary of Validation Parameters of HPTLC Method

Particulars	Specifications
Make	CAMAG , Switzerland
Applicator	Camag Linomat 5, Semi automatic application, band application by spray on technique (2-500mL).
Syringe	Hamilton 100 ml HPTLC syringe.
Stationary Phase	Silica Gel 60 G F_{254} coated on aluminium sheet. (Merck, Germany)
Chamber	Camag twin trough glass chamber (10cm´10cm & 20cm´10cm).
Scanner	Camag TLC Scanner 3, scan speed up to 100mm/s, Spectral range 190-800nm.
Software	WinCATS Planner Chromatography Manager, version 1.3.4.
Documentation	Camag Reprostar 3 with digital camera for 254 nm, 366 nm and visible light source.
UV Cabinet	Camag UV cabinet with dual wavelength UV lamp 254 & 366 nm.
Detection Wavelength	ENAL - 215 nm
	HCTZ - 270 nm
	PARA - 245 nm
Mobile Phase	Chloroform : Methanol : Toluene : Ethyl acetate
	(20 : 10 : 40 : 30, v/v/v/v)
Rf Value	ENAL - 0.20 ± 0.04
	HCTZ - 0.55 ± 0.03
	PARA - 0.72 ± 0.02

The developed HPLC method is simple, precise, accurate and reproducible and can used for simultaneous determination of enalapril maleate, hydrochlorothiazide, paracetamol in tablets. The method was validated as per ICH guidelines.

CONCLUSION:

As a result, simple, rapid and economical method for the simultaneous analysis of multicomponent formulation, which doesn't require extraction or separation of the analyte from themselves or from the excipients, becomes necessary for the pharmaceutical industry. By keeping all this in mind in the present study a new, simple, rapid, economic, accurate and selective, HPTLC method has been developed for simultaneous quantitative estimation of Enalapril maleate, Hydrochlorothiazide and Paracetamol in bulk and tablet dosage form.

Mobile phase selected for analysis was Chloroform: Methanol: Toluene: Ethyl acetate (20: 10: 40: 30 % v/v/v/v). The retention values for ENAL, HCTZ and PARA were found to 0.2.0.55 and 0.72 respectively.

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