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NOTE

RP-HPLC and HPTLC Estimation of Tramadol Hydrochloride and Paracetamol in Combination

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Two chromatographic methods for the estimation of tramadol and paracetamol were developed. RP- HPLC method used mobile phase consisted of KH_2PO_4 (0.1 M, pH 5.5): methanol (45:55 % v/v) and drugs monitored by UV detector. Valdecoxib was used as an internal standard. The elution order was 2.6, 5.9 and 6.5 min, respectively for paracetamol, tramadol and valdecoxib. HPTLC used a precoated silicagel G_{60} F_{254} sheets and mobile phase of ethyl acetate, toluene and ammonia and detected at 273 nm. The R_f values were 0.28 ± 0.02 and 0.57 ± 0.01 for tramadol and paracetamol, respectively. Both methods were validated as per ICH guidelines proved the suitability of the method.

Key Words: RP-HPLC, HPTLC, Tramadol hydrochloride, Paracetamol.

Tramadol[1,2] and paracetamol[1,2] are available in combined dosage form to act against acute pain. They show powerful synergistic effect as centrally acting analgesic. Many analytical methods[3-6] are available for the estimation of tramadol and paracetamol individually or in combination with other drugs. No analytical methods available for this combination. Hence the present paper aims at reporting two chromatographic procedure which can separate and quantity in tablets combining tramadol hydrochloride (37.5 mg) and paracetamol (325 mg) in combined dosage form.

Paracetamol and tramadol were procured as gift sample and tablet of this combined drugs were purchased from local market. All chemicals and reagent used were of AR/HPLC grade. Silicagel G_{60} F_{254} precoated aluminium plates with thickness of 200 mm was from E. Merck, Germany. A Shimadzu VP. series HPLC system with PDA detector and CAMAG HPTLC system with Linomat V applicator were used for the HPLC and HPTLC methods.

RP-HPLC Method

Chromatographic conditions: The column used was phenominex luna C_{18}, 250 × 4.6 mm i.d, 5µ particle size. The mobile phase used was 0.1 M

KH_2PO_4 (pH 5.5): methanol in 45:55% (v/v). The mobile phase was filtered through 0.45 µ cellulose membrane and degassed. Mobile phase was pumped at 1 mL/min. A 20 µL solution was injected in the isocratic system. The internal standard and was valdecoxib elutes monitored at 273 nm.

Preparation of standard and sample solutions: Tramadol (10 mg) and 90 mg of paracetamol were dissolved in methanol and diluted to 100 mL with same. A solution of valdecoxib (200 µg/mL) prepared in methanol. The mixture standard and internal standard were diluted appropriately to get 1-5 µg/mL of tramadol and 8-40 µg/mL of paracetamol.

20 Tablets were taken and average weight calculated. A quantity of powdered tablet equivalent to 10 mg of tramadol was taken and then added with methanol standard extracted with methanol (3 × 20 mL). Further filtered and diluted and used as sample solution.

A 20 mL of each standard and sample were injected in chromatographic system. From the peak area ratio of drugs/internal standard the amount present in tablet was calculated and shown in Table-1.

TABLE-1
ESTIMATION OF TRAMADOL AND PARACETAMOL
BY RP-HPLC AND HPTLC

Drug	Label claim (mg/tab)	Amount estimated (mg/tab)		Label claim* (%)		RSD (%)	
		HPLC	HPTLC	HPLC	HPTLC	HPLC	HPTLC
Tramadol	37.5	36.92 ± 0.32	36.89 ± 0.53	98.45	98.37	0.92	0.36
Paracetamol	325	324.77 ± 0.07	321.08 ± 0.41	99.93	98.79	1.07	1.46

*An Average of ± SD of 6 observations.

HPTLC Method

Chromatographic conditions: Various solvent systems were evaluated to arrive at an optimum resolution of two drugs. The solvent system consisting of ethyl acetate, toluene and ammonia (6:4:0.1, v/v/v) gave compact dense well resolved spots of the drugs from the mixture. The chamber was saturated for 15 min. Sample was applied at constant rate of 0.16 µL/s having scan speed of 10 mm/s with 16 mL band width and plate was scanned at 254 nm.

Standard and sample preparation: An accurately weighed quantity of 10 mg of tramadol and 90 mg of paracetamol was dissolved in 10 mL (1 µg/mL). It was diluted so that the solution contain 0.1 and 0.9 µg/mL of tramadol and paracetamol, respectively. 1-5 µL of this solution was spotted on plates, developed, dried & densitometrically scanned at 254 nm. Similarly

prepared sample solution (formulation) was also analyzed as above and the amount of tramadol and paracetamol present is tablet was calculated using calibration curve of respective drug (Table-1).

The validation procedures were carried are as per ICH guidelines. The various parameters and their study result obtained by HPLC and HPTLC methods are shown in Table-2.

TABLE-2
VALIDATION PARAMETERS OF TWO METHODS

Parameter	RP-HPLC		HPTLC	
	Tramadol	Paracetamol	Tramadol	Paracetamol
Theoretical plates (n)	6535	5242	1243	3785
LOD (ng)	90	8	30	50
LOQ (ng)	250	100	100	500
Recovery (%)	99.86	98.35	99.66	99.84
RSD (%)	0.567	0.791	1.22	1.82
Precision RSD (%)	0.351	1.05	1.11	1.35

The chromatographic methods developed were linear and reproducible in their results. A comparison of two methods shown is Table-3. The HPTLC method is more sensitive then HPLC, but separation efficiency was much higher in HPLC. The % RSD of methods showed < 2, confirming the suitability of the method for the purpose. To conclude, both the methods are suitable for evaluating tramadol and paracetamol in raw material and dosage forms.

TABLE-3
COMPARISON OF TWO METHODS

Parameter	RP-HPLC		HPTLC	
	Tramadol	Paracetamol	Tramadol	Paracetamol
Linearity (µg/mL)	1-5	8-40	0.1-0.5	0.9-4.5
Label claim (%)	98.45	99.93	98.37	98.79

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