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A NEW RP-HPLC METHOD FOR SIMULTANEOUS ESTIMATION OF TOLCAPONE AND QUINAPRIL IN ITS PURE AND PHARMACEUTICAL DOSAGE FORM

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Keywords:

Tolcapone and Quinapril, Validation, stability-indicating method, degradation products

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ABSTRACT: A short selective, precise, accurate, and sensitive method for the estimation of Tolcapone and Quinapril was done by RP-HPLC. The assay of Tolcapone and Quinapril was performed with tablets, and the % assay was found to be 100.19 and 100.45, which shows that the method is useful for routine analysis. The linearity of Tolcapone and Quinapril was found to be linear with a correlation coefficient of 0.999 and 0.999, which shows that the method is capable of producing good sensitivity. The acceptance criteria of precision percent RSD should be not more than 2.0%, and the method show precision 0.2 and 0.7 for Tolcapone and Quinapril, which shows that the method is precise. The acceptance criteria of intermediate precision are RSD should be not more than 2.0%, and the method show precision 0.3 and 0.7 for Tolcapone and Quinapril, which shows that the method is repeatable when performed in different days also. The LOD and LOQ for Tolcapone were found to be 3.07 and 9.98, and LOD and LOQ for Quinapril were found to be 2.95 and 10.00. Therefore, this method can be adopted to estimate Tolcapone as well as Quinapril in other pharmaceutical formulations.

INTRODUCTION: Tolcapone is a drug that inhibits the enzyme catechol-O-methyl transferase (COMT) [1]. It is used in the treatment of Parkinson's disease as an adjunct to levodopa/carbidopa medication [2]. It is a yellow, odourless, non-hygroscopic, crystalline compound. Tolcapone is soluble in organic solvents such as ethanol, DMSO, and dimethylformamide (DMF), which should be purged with an inert gas. Tolcapone is sparingly soluble in aqueous buffers [3]. Tolcapone is a reversible inhibitor of catechol-O-methyltransferase (COMT; Ki= 0.27 nM for human recombinant COMT), an enzyme that degrades catecholamines, including dopamine and L-DOPA.

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Tolcapone crosses the blood-brain barrier and can inhibit both peripheral and central COMT activity. By inhibiting COMT, tolcapone increases L-DOPA efficacy and reduces L-DOPA-induced motor complications in animal models of Parkinson's disease [4, 5].

Quinapril is the ethyl ester prodrug of the non-sulfhydryl angiotensin-converting enzyme inhibitor quinaprilat. It is used to treat hypertension and heart failure [6, 7]. ACE inhibitors are commonly used as first-line therapy in the treatment of hypertension, along with thiazide diuretics or beta-blockers [8]. Quinapril is indicated for the treatment of hypertension and as an adjunct therapy in the treatment of heart failure. Quinapril prevents the conversion of angiotensin I to angiotensin II by inhibiting of angiotensin-converting enzyme and reduces bradykinin's breakdown. Reduced levels of angiotensin II lead to lower levels of PAI-1, reducing the risk of thrombosis, especially after

myocardial infarction. Quinapril hydrochloride is white to off-white amorphous powder that is freely soluble in aqueous solvents [9, 10].

The therapeutic efficacy of Quinapril can be increased when used in combination with Tolcapone. Only few methods were reported for the simultaneous estimation of tolcapone and quinapril by HPLC [11, 12]. Hence we had made an attempt to develop a simple, accurate and precise RP-HPLC method for the simultaneous estimation of tolcapone and quinapril.

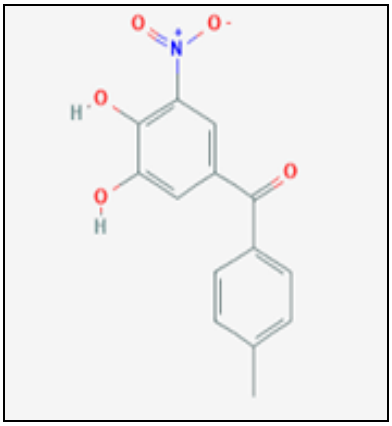

FIG. 1: TOLCAPONE

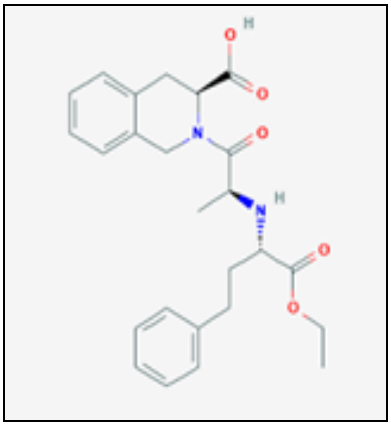

FIG. 2: QUINAPRIL

MATERIALS AND METHODS: Gift samples of tolcapone and quinapril were received from pharma train lab, Hyderabad. KH_2PO_4 was purchased from Final chemicals, whereas water, methanol for HPLC, and orthophosphoric acid were purchased from LICHROSOLV, Merck.

Instrumentation: Waters HPLC (2695 separation module) was used for the separation of tolcapone and quinapril. UV/VIS spectrophotometer (LAB-INDIA UV 12.500^{+}) was used for detection. Instruments such as; pH meter used was of Adwa - AD 10100, and the weighing machine was of Afcoset ER-1000A.

Preparation of Buffer and Mobile Phase:

Preparation of 0.1% OPA: Pipette 1ml of orthophosphoric acid dissolved in 1000 ml of HPLC water Ph was adjusted up to 3.0. The final solution was filtered through a 0.44 µm Membrane filter and sonicate it for 10 min.

Preparation of Mobile Phase: Accurately measured 300 ml (30%) of above buffer and 700 ml of Methanol HPLC (30%) were mixed and degassed in an ultrasonic water bath for 10 minutes and then filtered through 0.45 µ filter under vacuum filtration.

Diluent Preparation: The Mobile phase was used as the diluent.

Standard Solution Preparation: Accurately weigh and transfer 50 mg of Tolcapone and 20 mg of Quinapril working standard into a 100 ml clean, dry volumetric flask; add about 7 mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 1.5 ml of the above stock solutions into a 10ml volumetric flask and dilute up to the mark with diluent.

Sample Solution Preparation: Accurately weigh 10 tablets crush in mortor and pestle, and transfer equivalent to 50 mg of Tolcapone and 20 mg Quinapril sample into a 100 mL clean, dry volumetric flask; add about 7 mL of Diluent and sonicate it up to 15 mins to dissolve it completely and make volume up to the mark with the same solvent. Then it is filtered through a 0.45-micron Injection filter. (Stock solution)

Further pipette 1.5ml of Tolcapone and Quinapril from the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent.

Procedure: Inject 20 µl of the standard, sample into the chromatographic system and measure the areas for Tolcapone and Quinapril peaks and calculate the % Assay by using the formulae.

Experimental:

Optimized Chromatographic Conditions:

Instrument used	:	Waters HPLC with auto sampler and UV detector
Temperature	:	Ambient
Column	:	Agilent Eclips (4.6 × 150mm, 5µm)
Buffer	:	0.1% OPA
pH	:	3.0
Mobile phase	:	30% buffer 70% Methanol
Flow rate	:	1 ml per min
Wavelength	:	240 nm
Injection volume	:	20 µl
Run time	:	10 min

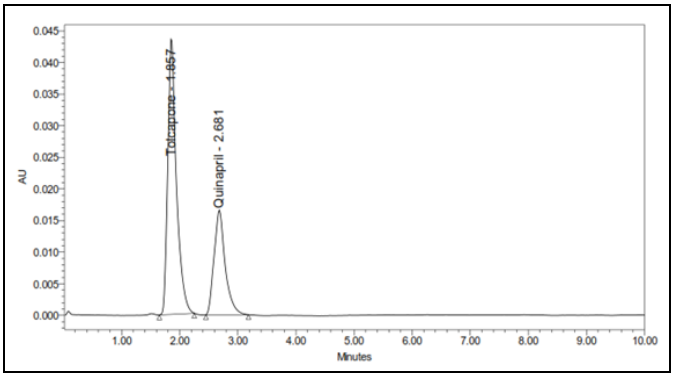

FIG. 3: STANDARD CHROMATOGRAM OF TOLCAPONE AND QUINAPRIL

System Suitability: All the parameters were evaluated by performing system suitability studies. The recorded responses for suitability studies are depicted in **Table 1**.

TABLE 1: RESULTS OF SYSTEM SUITABILITY PARAMETERS

S. no.	Name	RT(min)	Area (µV sec)	Height (µV)	USP resolution	USP tailing	USP plate count
1	Tolcapone	1.857	446832	43573		1.46	4725..92
2	Quinapril	2.681	218536	16544	3.18	1.29	6256.39

TABLE 2: RESULTS OF LINEARITY OF TOLCAPONE AND QUINAPRIL

S. no.	Tolcapone		Quinapril	
	Concentration (µg/ml)	Area	Concentration (µg/ml)	Area
1	25	148475	10	71914
2	50	286753	20	140828
3	75	445725	30	215732
4	100	596836	40	286753
5	125	745622	50	357562

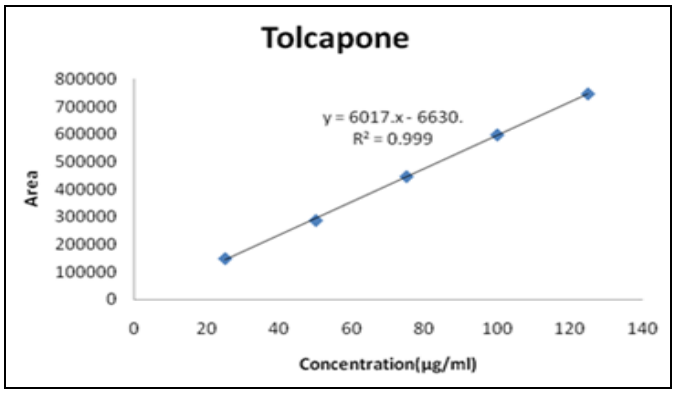

FIG. 4: CALIBRATION GRAPH FOR TOLCAPONE

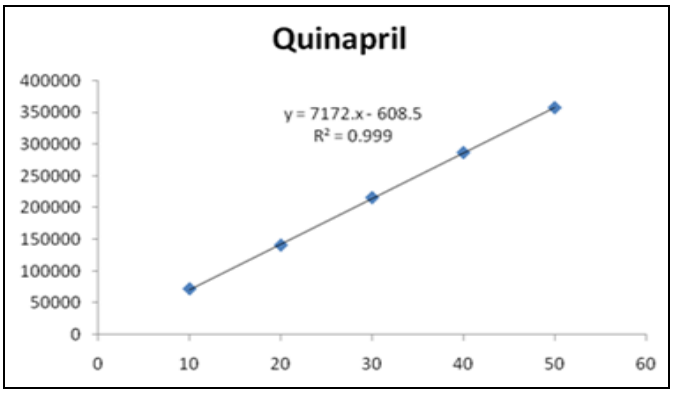

FIG. 5: CALIBRATION GRAPH FOR QUINAPRIL

TABLE 3: RESULTS OF PRECISION FOR TOLCAPONE

Injection	Area
Injection-1	448662
Injection-2	446873
Injection-3	446352
Injection-4	447562
Injection-5	447529
Injection-6	446244
Average	447203.7
Standard Deviation	907.4
%RSD	0.2

TABLE 4: RESULTS OF PRECISION FOR QUINAPRIL

Injection	Area
Injection-1	218753
Injection-2	214829
Injection-3	216426
Injection-4	218452
Injection-5	216468
Injection-6	217567
Average	217082.5
Standard Deviation	1468.9
%RSD	0.7

TABLE 5: ACCURACY (RECOVERY) DATA FOR TOLCAPONE

% Concentration (at specification Level)	Area	Amount Added (mg)	Amount Found (mg)	% Recovery	Mean Recovery
50%	225703.3	25	25.17	100.69	100.39
100%	448469.7	50	50.02	100.04	
150%	675482.7	75	75.34	100.45	

*Average of three determinations

TABLE 5: ACCURACY (RECOVERY) DATA FOR QUINAPRIL

% Concentration (at specification Level)	Area	Amount Added (mg)	Amount Found (mg)	% Recovery	Mean Recovery
50%	109553.3	10	10.04	100.44	100.39
100%	219228.7	20	20.10	100.50	
150%	327988.3	30	30.07	100.24	

*Average of three determinations

TABLE 7: RESULTS OF LOD

Drug name	Baseline noise (µV)	Signal obtained (µV)	S/N ratio
Tolcapone	56	172	3.07
Quinapril	56	165	2.95

TABLE 8: RESULTS OF LOQ

Drug name	Baseline noise (µV)	Signal obtained (µV)	S/N ratio
Tolcapone	56	565	9.98
Quinapril	56	556	10.00

Degradation Studies:

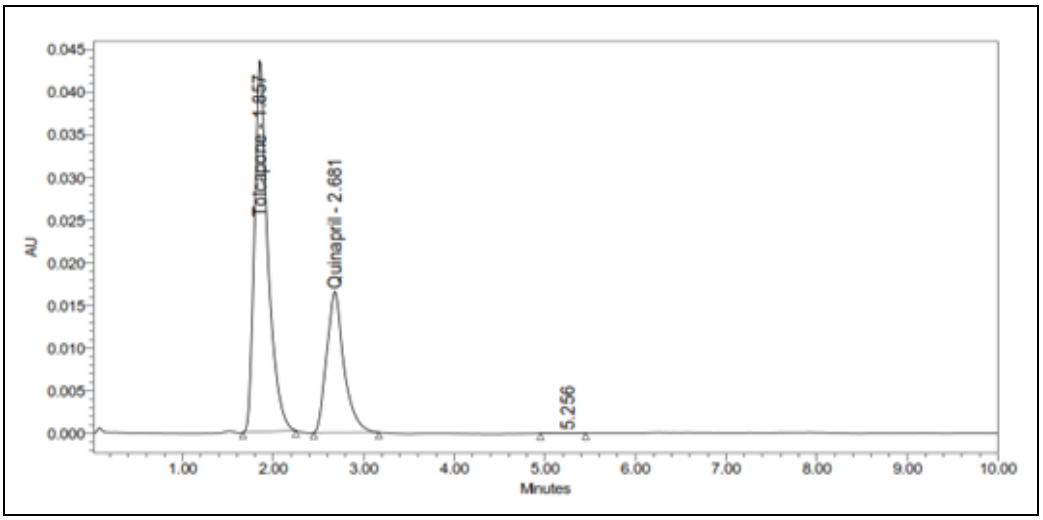

FIG. 6: CHROMATOGRAM SHOWING ACID DEGRADATION

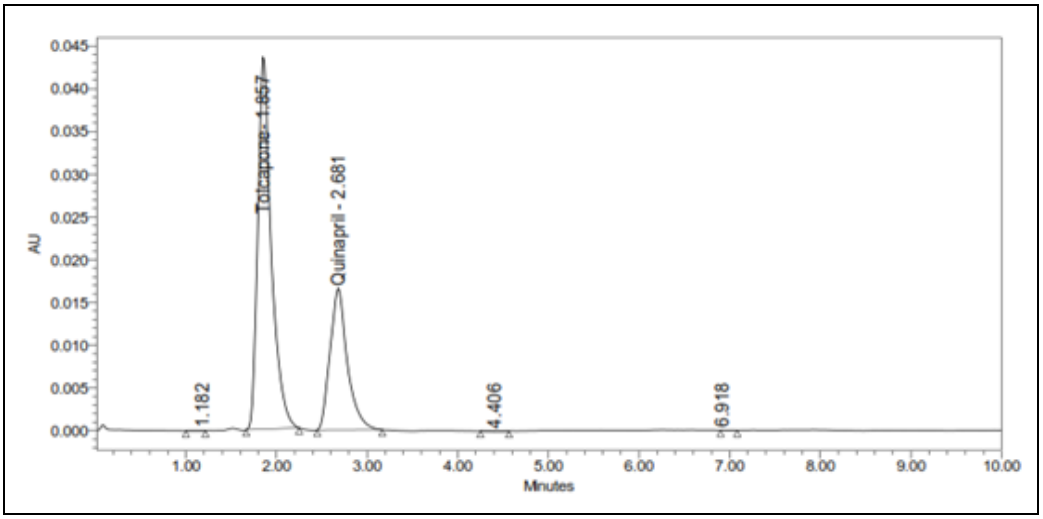

FIG. 7: CHROMATOGRAM SHOWING BASE DEGRADATION

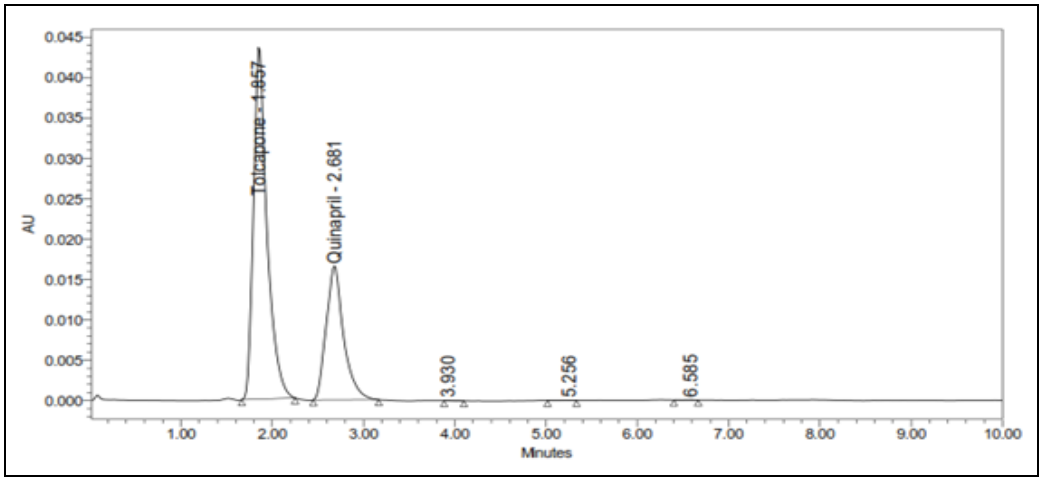

FIG. 8: CHROMATOGRAM SHOWING PEROXIDE DEGRADATION

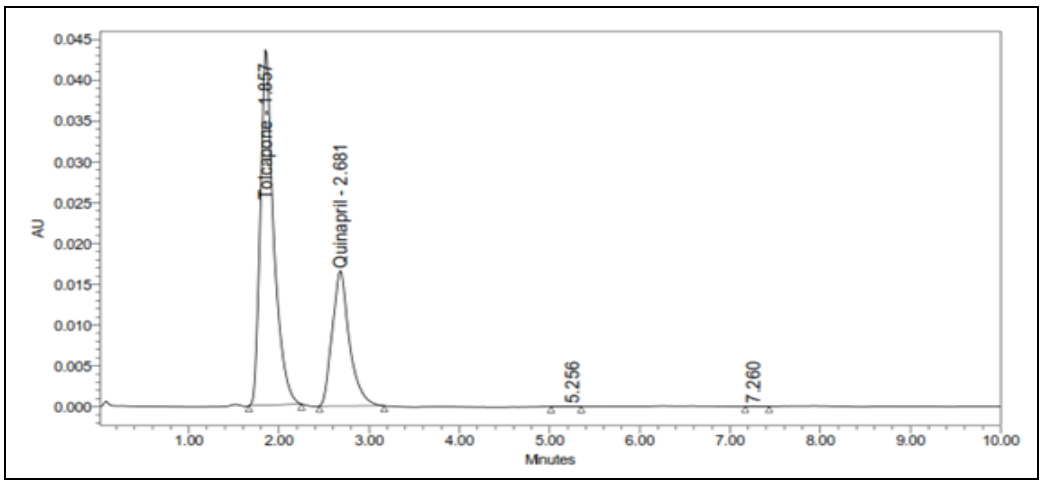

FIG. 9: CHROMATOGRAM SHOWING THERMAL DEGRADATION

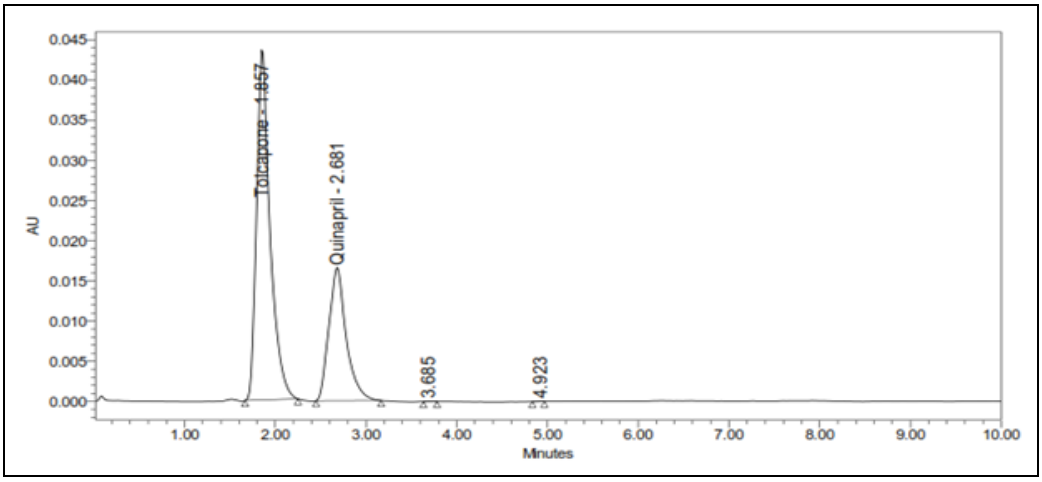

FIG. 10: CHROMATOGRAM SHOWING PHOTO DEGRADATION

TABLE 9: RESULTS FOR STABILITY OF TOLCAPONE AND QUINAPRIL

Sample Name	Tolcapone		Quinapril	
	Area	% Degraded	Area	% Degraded
Standard	447408.3		217707	
Acid	436522	2.43	207853	4.53
Base	428673	4.19	196762	9.62
Peroxide	439657	1.73	206752	5.03
Thermal	430876	3.70	199672	8.28
Photo	421862	5.71	195534	10.18

TABLE 10: RESULTS OF ASSAY FOR TOLCAPONE AND QUINAPRIL

	Label Claim (mg)	% Assay
Tolcapone	100	100.19
Quinapril	40	100.45

SUMMARY AND CONCLUSION: From the above, it can be concluded that all validation parameters such as precision, accuracy, linearity and Ruggedness met the predetermined acceptance criteria as mentioned in ICH guidelines. The robustness limit for mobile phase variation and flow rate variation is well within the limit; the % degradation results are in limits. This shows that the method is having good system suitability and precision under a given set of conditions.

Hence, it can be concluded that the developed RP-HPLC method is accurate, precise, rapid, and selective and can be employed successfully for the estimation of tolcapone and quinapril in bulk and pharmaceutical dosage forms.

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CONFLICTS OF INTEREST: There are no conflicts of interest.

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