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A new sensitive and robust method development for estimation of tolcapone and quinapril in the bulk and formulations

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Abstract



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Tolcapone and Quinapril are anti-hypersensitive drugs and, in combined dosages, are effective in managing hypertension. The RP-HPLC method was developed using OPA and Acetonitrile in 50:50 v/v as Mobile phase and 250*4.6mm, 5 μ RP-HPLC column measured with a wavelength of 240nm. The HPLC system was fixed with a flow rate of 1.0ml/min; Both drugs, TOLCO and QUINA, were successfully detected at 2.153 and 3.203 min, respectively. The validation of the method as per ICH Linearity r^2 lies at 0.999, and Precision, system suitability, and selectivity RSD values are within permissible limits. The accuracy of the process was found to be 99.73 and 99.52 for TOLCO and QUINA, respectively. The LOD 0.72 and 0.3 μ l/ml and LOQ 0.84 and 0.13 μ l/ml. The robustness and degradation studies show that the selected method is acceptable per the Guidelines.

Keywords:

Tolcapone,
Quinapril,
RP-HPLC,
Simultaneous Estimation

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INTRODUCTION

Tolcapone (TOLCO) is a COMT protein inhibitor used in Parkinson's disorder. It is a yellow, hygroscopic crystalline powder used as an adjuvant for Levodopa, and it is soluble in DMF and DMSO [1][2][3][4] and Quinapril (QUINA) can be used to treat congestive heart failure and

inhibits the ACE enzyme. Quinapril prevents the conversion of angiotensin I to angiotensin II by inhibiting the ACE enzyme and eliminating more sodium from the body, thereby reducing the severity of hypertension [5][6][7]. Quinapril and tolcapone in combined dosages are approved by the FDA, but their combination is effective in treating hypertension and myocardial infarction. The clinical literature shows their combination effectively manages hypertension [8][9][10][11]. An attempt is made to develop the RP-HPLC method, and the developed method is validated as per the guidelines of ICH Q2(R1).

MATERIALS

Tolcapone and Quinapril were procured from Yarrow Chemicals, Mumbai. The Solvents and other chemicals were procured from the chemical vendor with HPLC grade. Potassium dihydrogen

phosphate, Methanol, Acetonitrile, and orthophosphoric acid HPLC grade chemicals.

Instruments: The Waters HPLC with Empower 2695 software integrates peaks. The UV-visible spectrophotometer Elico SL 210, pH meter, and ATY 224 digital balances were used to develop and validate this method. All the instruments were calibrated as per SOP and ICH guidelines.

Preparation of Mobile Phase and Buffer:

Preparation of 0.025 M Potassium Dihydrogen ortho Phosphate buffer: weigh an amount of 3.4 gm of KH_2PO_4 , which did at 60°C for 30 min before dissolving and take 1000 ml Volumetric flask filled with 700ml of HPLC grade water and add to it, add drop by drop of OPA until pH adjusts to 3.0. this solution is filtered and stored in a calm and dark place.

Preparation of Mobile Phase: Take 500 ml of the above buffer and 500 ml of Acetonitrile in a 1000 ml beaker and sonicate the solvent to remove dissolved gases from the mobile phase. After sonication, keep the solvent in a calm and dark place.

Standard solution preparation: 99.98% purity of tolcapone 100 mg and 99.89% of Quinapril 40 mg weighed respectively in a 100 ml volumetric flask and dissolved in Mobile phase sonicate the flask to dissolve, take out 1.0 ml and dissolve in another 10 ml volumetric flask and the resultant solution yields 100 ppm and 40 ppm of TOLCO and QUINA respectively.

Sample solution preparation: an equivalent weight of Quinapril 40 mg and tolcapone 100mg tablet powder dissolved in a 100 ml standard flask and dissolved in Mobile phase and sonicated in a sonicator for 15 min to dissolve the drug and undissolved part of tablet powder is removed by passing through the vacuum pump using 2.5 µ filter aid. Take 1 ml of filtrate and dissolve in another 10 ml of standard flask to obtain a similar concentration as that of standard.

Procedure: Injecting 20 µl of standard and sample solutions into the HPLC system individually by fixing the PDA detector at 240 nm. The peak area, height, retention time, tailing, and fronting of the peak were measured for TOLCO and QUINA, respectively, and an assay was conducted with the marketed product.

Optimization of Method:

- The instrument used: awas
- Temperature: Ambient (25°C)
- Mode of separation: Isocratic mode
- Column: Inertsil ODS long column
- Buffer: 0.25 M dihydrogen potassium phosphate
- Solvent phase: Buffer and Acetonitrile 50:50 ratios
- Stream flow: 1 ml per min
- Detection WL: 240 nm
- Infusion volume: 20 µl
- Run time: 8 min

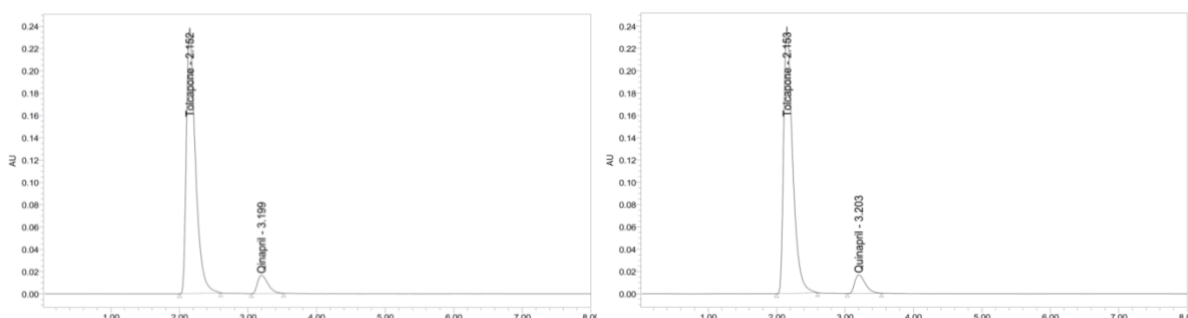


Figure 1 a) Standard Chromatogram b) Sample chromatogram

Table 1

S No	Name	RT	Area	Height	USP Plate	USP tailing	Resolution
1	Tolcapone	2.153	2194729	239798	3304.15	1.15	
2	Quinapril	3.203	176033	16857	2123.90	1.46	4.07

Table 2

Validation Parameter	Tolcapone	Quinapril	Acceptance
System Suitability - RSD	0.4%	0.1%	LT 2%
Precision	0.4%	0.1%	LT 2%
Intermediate Precision	0.9%	0.1%	LT 2%
Accuracy - 50,100,150%	99.73%	99.52%	95 - 105%
LOQ - s/n	0.72	0.84	
LOD - s/n	0.3	0.13	
Change in flow rate - plate count	3313	3730	GT 2000
Change in Org Phase - Plate count	3309	3134	GT 2000
Acid degradation	6.62%	6.60%	LT 10%
Base degradation	9.66%	8.54%	LT 10%
Peroxidation	9.26%	8.60%	LT 10%
Thermal degradation	9.26%	8.62%	LT 10%
Photolytic degradation	6.66%	7.07%	LT 10%
Essay	100.26	99.29	90-110%
Linearity	0.999	0.999	0.99-1.00

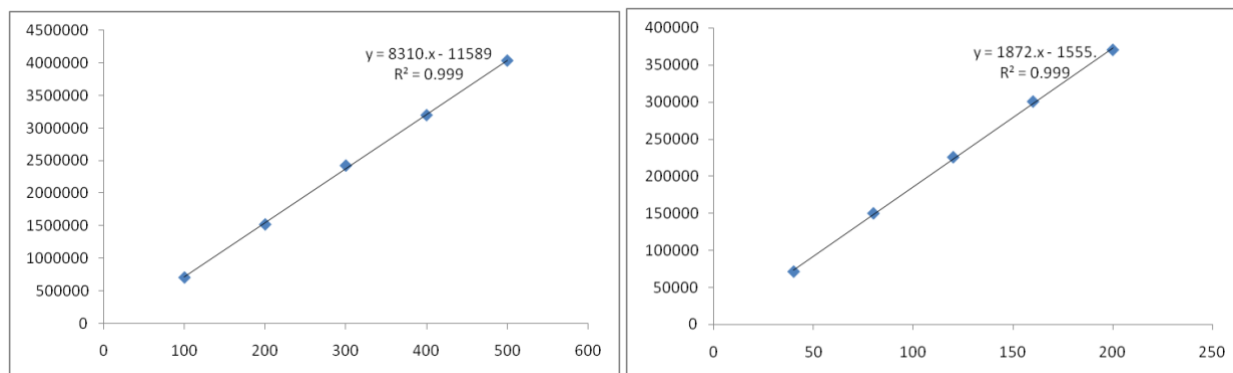


Figure 2 a) Linearity of Tolcapone b) Linearity of Quinapril

Validation:

[12][13][14][15][16][17][18][19][20]

System Suitability: 6 replicate injections were protruded into the HPLC injector system, calculated Mean, SD, and RSD, and the results with ICH analytical validation guidelines.

Precision: 6 similar concentrations of TOLCO and QUINA standard drugs were injected into the HPLC and calculated as similar to system suitability.

Intermediate Precision: Intermediate Precision is conducted between the hours of the same day at different time intervals.

Robustness: The robustness was measured by the change in analyst, change in organic mobile phase concentration, change in flow rate, and change in temperature and system conditions as lied by ICH guidelines.

Accuracy: Accuracy measures the nearness of the experiment with actual values. It was conducted using three different conceptions of standard solutions: 80,100 and 120%.

LOD: the minimum concentration of the drug to be detected using optimized chromatographic conditions using the s/n ratio method.

LOQ: The minimum concentration of the drug is to be quantified using the optimized chromatographic conditions using the s/n ratio method.

Linearity: a series of standard solutions were made using standard stock solution; the linearity graph was constructed for both drugs individually, the correlation was calculated, and it was found 0.999 for both.

RESULTS

SUMMARY AND CONCLUSION

The method optimized for its regular analysis by waters HPLC and the PDA detector set as 240 nm, the column dimension used as Inertsil ODS 4.6*250 mm, 5 μ particle size, the flow rate was maintained as 1.0 ml/Min, and the run time is 8.0 Min. The mobile phase was selected for pH 3.0, made with Dihydrogen potassium Phosphate, and pH was adjusted with orthophosphoric acid solutions and Acetonitrile in proportion to 50:50 v/v ratios. The standard Tolcopone and Quinapril retention times were obtained at 2.153 and 3.203 Minutes, respectively.

The validation parameters, such as system suitability, linearity, Precision, accuracy, and sensitivity, such as LOD, LOQ, and all other parameters, were verified using the selected method. The method was validated according to ICH guidelines, and all are within the limits of the guidelines. Hence, the method developed was simple and precise for regular analysis of Tolcopone and Quinapril in the form of tablets.

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Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

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