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An HPLC method for the Simultaneous estimation of Risperidone and Trihexyphenidyl hydrochloride from Bulk and Dosage forms.

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Abstract

A simple, fast and precise reverse phase high performance liquid chromatographic method developed for the simultaneous determination of risperidone and trihexyphenidyl hcl in its tablets form. C_{18} phenomenex Gemini column 250mm x 4.6mm (l x d) in isocratic mode with mobile phase buffer: Acetonitrile: methanol (50:30:20) % v/v were used. The flow rate was 1 ml/min. Linearity for risperidone and trihexyphenidyl hcl were in the range of 96.96 mcg/ml – 145.44mcg/ml and 65.60 mcg/ml – 98.4 mcg/ml respectively. Amount found of risperidone and trihexyphenidyl hcl in sizodon plus was 3.034 mg/tab and 2.063 mg/tab respectively. Amount found of risperidone and trihexyphenidyl hcl in RI- plus was 3.016 mg/tab and 2.044 mg/tab respectively. Percentage recoveries obtained for risperidone and trihexyphenidyl hcl in sizodon plus were 100.87% and 102.49% respectively, percentage recoveries obtained for risperidone and trihexyphenidyl hcl in RI-plus were 100% and 101.65% respectively. The proposed method is accurate, precise, selective and rapid for the simultaneous estimation of risperidone and trihexyphenidyl hydrochloride in tablet dosage.

Key words: HPLC, Validation, Risperidone, Trihexyphenidyl hydrochloride

1. Introduction

Risperidone has exhibited good therapeutic efficacy against both positive and negative schizophrenic symptoms with low incidence of EPS. Chemically the drug is 3-[2-[4-(6- fluoro -1, 2-benzisoxazol -3-yl) -1 piperidinyl] ethyl] -6,7,8,9- tetrahydro – 2 methyl – 4 H – Pyrido [1, 2 – a] Pyrimidin – 4 – one.

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Several methods such as LC/ MS/ MS[1] , HPLC[2], LC-MS[3] have been reported in the literature. Trihexyphenidyl Hcl is used to treat all forms of Parkinsonism. This medicine may also be prescribed to control extrapyramidal disorders (except tar dive dyskinesia) due to central nervous system drugs. Chemically the drug is 1- cyclohexyl -1- phenyl -3 (1- piperidyl) propane -1- ol. Several methods such as HPLC[4], HPLTC[5], have been reported in the literature.

2. **Materials and methods**

HPLC pump isocratic LC 20 AT equipped with rheodyne injection volume 20 µl, uv – vis detector SPD – 20 A. Reference standard of risperidone and trihexyphenidyl hcl. Sizodon – plus (Sun pharmaceuticals), RI-plus (VGR bio Laboratories) were procured from market. Label claim of sizodon plus tablets is Risperidone-3mg and Trihexyphenidyl-2mg. Label claim of RI-Plus tablets is Risperidone-3mg and Trihexyphenidyl-2mg. Acetonitrile HPLC grade, water of HPLC grade, orthophosphoric acid HPLC grade, methanol HPLC grade, Trienthylamine HPLC grade reagents were used. Stationary Phase C_{18}, 5µ, phenomenex Gemini column 250mm x 4.6mm (LxD) was used.

0.3% orthophosphoric acid was prepared in water and adjusted the pH to 3.0 with triethylamine as buffer. 50ml of buffer was mixed with 30ml of Acetonitrile and 20ml of methanol to form 100ml of mobile phase, finally filtered through membrane filter 0.45mm micron degassed.

2.1. **Standard Stock Solution**

30.3mg of risperidone and 20.5mg of Trihexyphenidyl Hcl were taken in 50ml volumetric flask, dilute with little amount of mobile phase and the contents were shaken thoroughly and finally make up the volume to 50ml with the same mobile phase. 5ml of the above solution is transferred to a 25ml volumetric flask, dilute with little amount of mobile phase and the contents were shaken thoroughly and finally make up the volume to 25ml with the same mobile phase.

2.2. **Sample Solution**

10 tables were weighed and crushed to obtain a fine powder and transferred to a 50ml volumetric flask. Little amount of mobile phase was added and the contents were shaken thoroughly and finally make up the volume to 50ml. 5ml of the above solution is taken and transferred a 25ml volumetric flask. Little amount of mobile phase was added and the contents were shaken thoroughly and finally make up the volume to 25ml.

3. **Results and discussion:**

3.1. **Assay:** 20µl standard stock solution and sample solutions (n=4) were injected in to an injector of liquid chromatograph. From the peak area of risperidone and trihexyphenidyl Hcl, the amount of drugs in samples (n=4) were computed
A typical HPLC chromatogram of Risperidone and Trihexyphenidyl hydrochloride as shown in fig 1. In replicate analysis n=4 of two drugs by the proposed method the content of risperidone and trihexyphenidyl Hcl in sizodon plus were 3.034 mg / tab and 2.063mg/tab respectively. The content of risperidone and trihexyphenidyl Hcl in RI-plus were 3.016mg/tab and 2.044mg/tab respectively. The results obtained by the proposed method were close to the label claim of both the drugs indicating that the method is precise and accurate.

3.2. **Linearity Study:** In to a series of five standard measuring flask, varying amount of standard stock solution of combination of risperidone and trihexyphenidyl Hcl was taken and made up to various concentrations of 96.98, 109.08, 121.20, 133.32, 145.44 mcg/ml (80, 90, 100, 110, 120%) for risperidone and 65.60, 73.80, 82.0, 90.2, 98.4 mcg/ml (80, 90, 100, 110, 120%) for trihexyphenidyl hcl, 20µl was injected from each flask. The peak area response of the solutions were recorded at 220nm. The plot of peak area versus the respective concentrations of risperidone and trihexyphenidyl Hcl were found to be linear in the range of 96.98 – 145.44mcg/ml and 65.60 – 98.4mcg/ml respectively with coefficient of correlation (r = 0.9999) and (r = 0.9998) respectively as shown in Fig.2.

3.3. **Accuracy:** Accuracy studies were performed at 80%, 100%, 120% spiked sample. Three replicates of each concentration were performed. The mean percentage recovery of risperidone and trihexyphenidyl hcl in sizodon plus were 100.87% and 102.49% respectively. The mean percentage recovery of risperidone and trihexyphenidyl hcl in RI-plus were 100.00% and 101.65% respectively. Since there is no significant difference between the theoretical and actual, the method is shown to be accurate and selective.

3.4.**Robustness:** Robustness mobile phase alter increasing 20% buffer, the value of retention time, number of theoretical plates, tailing factor for risperidone & trihexyphenidyl hcl were 4.457,2797,1.58 & 9.730,6690,1.14 respectively. Robustness mobile phase alter increasing 20% acetonitrile, the value of retention time, number of theoretical plates, tailing factor for risperidone & trihexyphenidyl hcl were 1.580,2581,1.48 & 3.543,3897,1.55. respectively. It shows the reliability of an analysis with respect to deliberate variations in method parameters.

3.5.**System Suitability:** System suitability tests were carried out on freshly prepared standard stock solution of risperidone and trihexyphenidyl Hcl and the parameters obtained with 20µl injection volume and standard stock solution(n=6) are shown in Table 1

4. **Conclusion:**

The proposed method is simple**,** precise and accurate for the simultaneous determination of risperidone and trihexyphenidyl hydrochloride in tablet dosage. In routine Quality control or in Test Laboratories, when we have this formulation to be analyzed, the method is best suited.

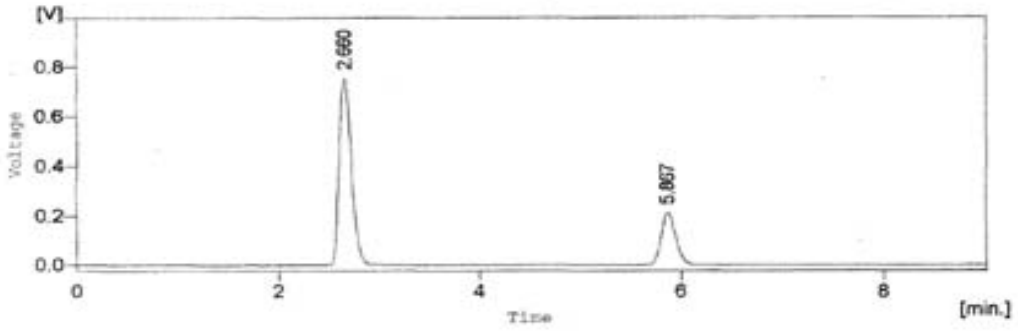

Fig. 1 Typical HPLC Chromatogram Of Risperidone & Trihexyphenidyl Hcl

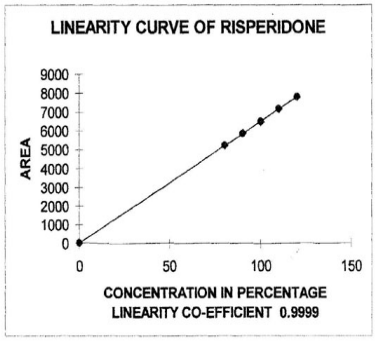

Fig .2 Typical Linearity curve of Risperidone and Trihexyphenidyl hydrochloride

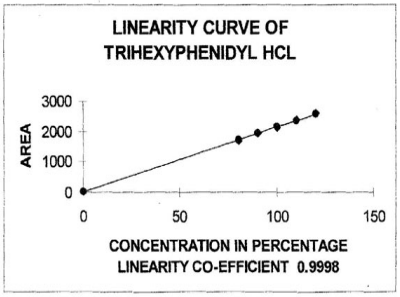

Table 1 System Suitability Parameters

Parameters	Risperidone	Trihexyphenidyl hcl
Retention time	2.685	5.912
Tailing factor	1.351	1.200
Theoretical plate	2161.83	7972.83
Peak area	6448.461	2188.988
RSD of peak area	0.31%	0.53%

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