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Absorption Correction Method For Estimation Of Risperidone And Trihexyphenidyl HCl In Combined Tablet Dosage Form

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Abstract: The aim of present work to develop validated UV-spectrophotometric absorption correction method for simultaneous estimation of Risperidone and Trihexyphenidyl HCL in combined pharmaceutical preparations. The method is based upon determination of Trihexyphenidyl HCL at 219 nm and Risperidone at 282 nm, in 0.1N HCL. Trihexyphenidyl HCL and Risperidone show linearity in the concentration range of 8-80 µg/ml and 4 -40 µg/ml respectively at their respective λmax 219.0 nm and 282 nm. The method was validated statistically.
***Keywords*:** Risperidone; Trihexyphenidyl HCL; absorption correction method.

INTRODUCTION:

Risperidone (RIS) is psychotropic agent used to treat schizophrenia, action of which is mediated through a combination of dopamine Type 2 (D_2) and serotonin Type 2 ($5HT_2$) receptor antagonism. It is a selective monoaminergic antagonist with high affinity for $5HT_2$, D_2 and H1 histaminergic receptors[1]. It belongs to chemical class of benzisoxazole derivative and 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 with molecular formula of $C_{23}H_{27}FN_4O_2$ and molecular weight of 410.49.

Literature survey revealed that various methods have been reported for estimation of RIS in biological matrices such as plasma with help of liquid chromatography (LC) [2,3] , LC with diode array detection [4], LC with tandem mass spectrometry [5,6,7] and LC with electrochemical detection [8]. Few stability-indicating methods have been reported for determination of RIS in bulk powder and tablets in presence of its degradation products [9,10] .

Benzhexol hydrochloride or Trihexyphenidyl hydrochloride (THP); 1-Cyclohexyl-1-phenyl-3-(1-piperidyl) propan-1-ol hydrochloride, is used to treat the stiffness, tremors, spasms, and poor muscle control of Parkinson's disease. Molecular formula of THP is $C_{20}H_{31}NO$. HCl and molecular weight of 337.9 [11]. .

THP is official in BP and USP NF [12,13]. Literature survey revealed that HPLC [14,15] methods have been reported for the estimation of Risperidone and Trihexyphenidyl individually and with other drugs in pharmaceutical dosage forms. Yet there was no spectrophotometric method reported for the simultaneous estimation of the RIS and THP in combined tablet dosage form. Therefore, it was thought worthwhile to develop simple, precise, accurate spectrophotometric method for simultaneous estimation of RIS and THP in combined tablet dosage form.

For this purpose marketed tablets RIDON PLUS -3 containing 3 mg of RIS and 2 mg of THP was used.

EXPERIMENTAL

Material and Method:

Double beam UV–visible spectrophotometer UV 2401 PC (Japan) Thermo, with 1cm UV matched quartz cells was used. Citizen Balance was used for experimental purpose. Pharmaceutical grade RIS (Batch No. TRS PP 9004) and THP (Batch No. PD/TH/0913) were supplied as a gift sample by Talent India, Ahmadabad, (Gujrat), India. The tablet dosage form (RIDON PLUS 3, Batch No. 06R13, Mfg. Dt. 05/09 and Exp. Dt. 11/11) was procured from the local market (Label claim: 3 mg RIS and 2 mg THP) marketed by KIVI Lab, Baroda.

Preparation of standard solution:

Risperidone stock standard solution:

An accurately weighed quantity of RIS 10 mg was transferred to the 100 mL volumetric flask and dissolved in 25 ml of 0.1N HCL and sonicate for 5 min. The volume was made up to the mark with 0.1N HCL (100 µg/mL).

Trihexyphenidyl HCL stock standard solution:

An accurately weighed quantity of THP 20 mg was transferred to the 100 mL volumetric flask and dissolved in 25ml of 0.1N HCL and sonicate for 5 min . The volume was made up to the mark with the 0.1N HCL (200 µg/mL).

Study of spectra and selection of wavelength:

The aliquot portions of stock standard solutions of RIS and THP were diluted appropriately with solvent to obtain concentration 20 µg/mL of each drug. The solutions were scanned in the range of 400 –200 nm against blank. The overlain UV absorbance spectrum of RIS and THP is shown Fig.1.

From the overlain spectrum shown in Fig.1, the wavelength 219 nm and 282.0 nm were selected for the estimation.

The RIS and THP obey Beer's law in the concentration range of 0 to 40 µg/ml and 0 to 80 µg/ml at selected wavelength as shown in Fig.2 and Fig.3.

Quantitative estimation of these drugs was carried out by using following formulae's.

$$Cy = A\ 282\ nm / a_y\ 282\ nm\ of\ RIS$$

$$A219 = Ay\ 219 + Ax\ 219$$

$$A219 = Cy \times a_{y\ 219} + Cx \times a_{x\ 219}$$

$$Cx = \frac{A219 - Cy \times a_{y\ 219}}{a_{x\ 219}}$$

Where,

Cx concentration (g /100ml) of THP

Cy concentration (g /100ml) of RIS

A282 nm and A219.0 nm are absorbance of mixture at 282 nm and 219.0 nm, respectively,

Ay219 nm and Ax 219.0 nm are absorbance of RIS and THP at 219.0 nm, respectively,

a_y 282 nm = Absorptivity of RIS at 282

a_y 219 nm and a_x 219 = Absorptivity of RIS and THP at 219

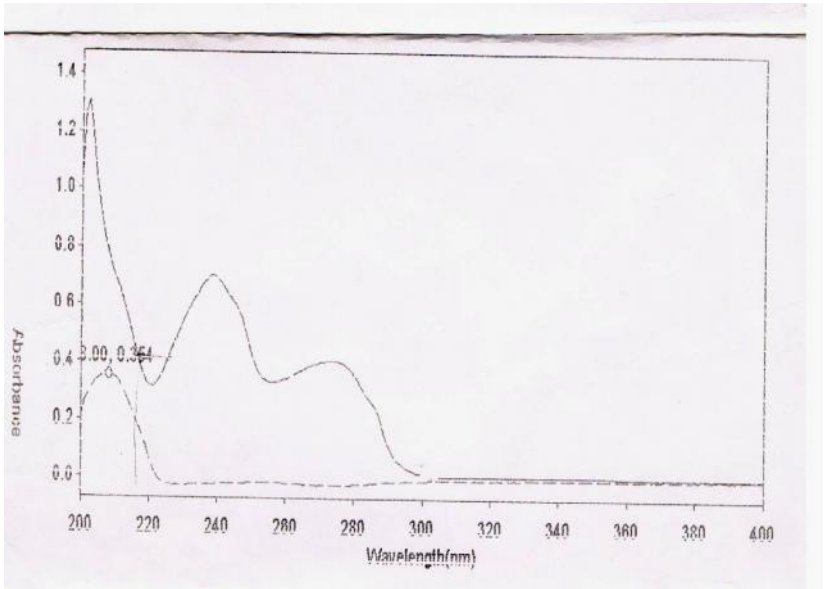

Fig.1: Overlain spectra of RIS and THP

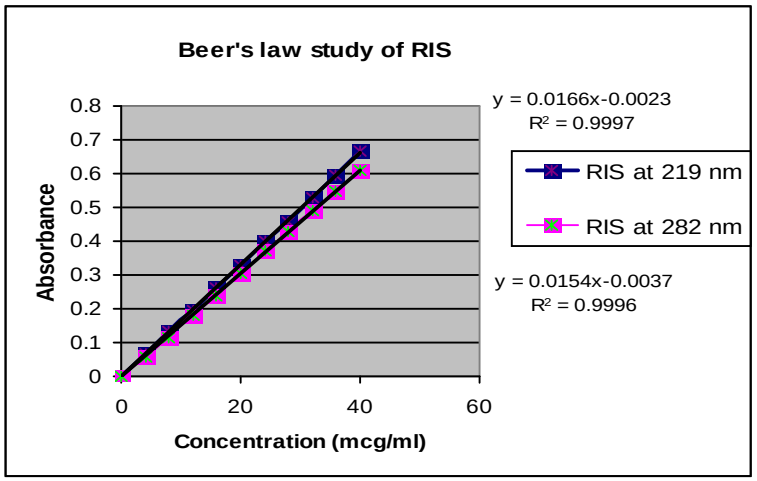

Fig.2: Plot of Beer-Lambert study for RIS at 219 and 282 nm

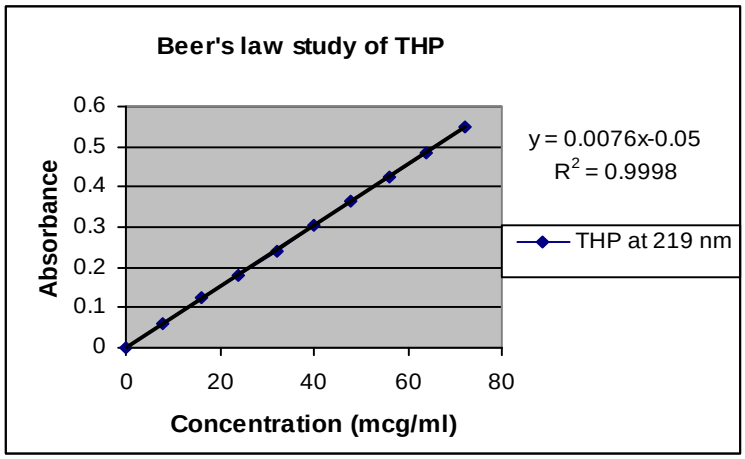

Fig.3: Plot of Beer-Lambert study for THP at 219 nm

Estimation of drugs in commercial tablet formulation

Twenty tablets were accurately weighed. Average weight of tablet was calculated. The tablets were reduced to fine powder and mixed thoroughly. A quantity of tablet powder equivalent to weight of one tablet was transferred to 100 mL volumetric flask and dissolved in 25 ml of solvent i.e. 0.1N HCL and sonicate for 5 min and volume was made to 100 mL with the same solvent to get final concentration of about 30 µg/mL RIS and 20 µg/mL THP. The solution was filtered through Whatman filter paper no. 41. The absorbance of sample solution was measured at 219 nm and 282 nm in 1 cm cell against blank.

Validation:

The proposed method was validated on the basis of parameters namely accuracy, precision, ruggedness, linearity and range. The accuracy of the proposed method was ascertained by carrying out recovery studies using standard addition method. The recovery study was performed to determine if there was any positive or negative interference from excipients present in the formulation. Precision of an analytical method is expressed as SD or RSD of a series of measurements. It was ascertained by replicate estimation of drug by the proposed method. Test for ruggedness was carried out by repeating the procedure under different conditions, i.e., on different days, at different time and by different analysts. Linearity and range study was done by preparing concentration in the range of 80 -120 % of test concentration and absorbance values were recorded at 219.0 nm and at 282.0 nm. The plot of linearity and range is shown in Fig.4.

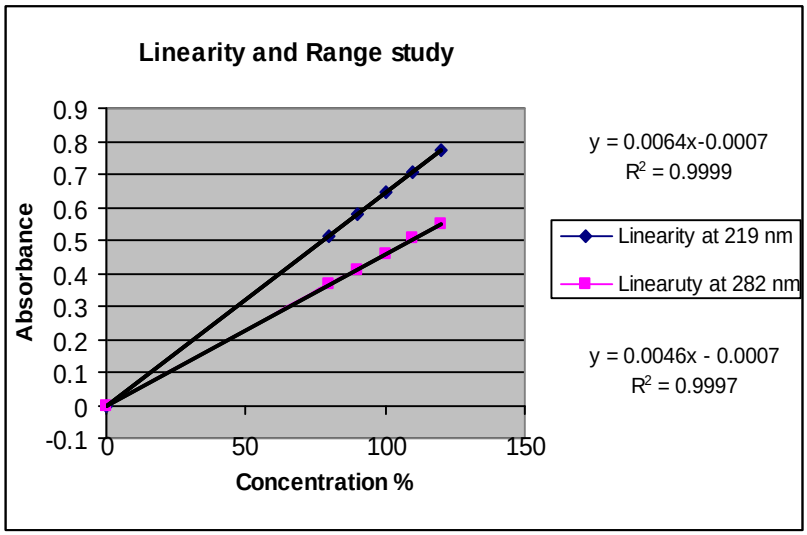

Fig. 4: Plot of linearity and range for RIS and THP

Table 1: Result of estimation of RIS and THP in Tablet formulation

Brand name. RIDON PLUS 3 Average weight =117.8 mg

Sr. No.	Weight of tablet powder (mg)	Absorbance		% Lable claim	
		A_1	A_2	RIS	THP
1	117.6	0.454	0.642	99.2	99.35
2	117.7	0.455	0.643	99.45	99.6
3	117.9	0.451	0.640	98.5	100.2
			Mean	99.05	99.71
			± S.D.	0.492	0.436
			C.V.	0.497	0.438

Table 2: Results of recovery studies of RIS and THP

Sr. No	Weight of tablet powder (mg)	Amount Added in µg.		Absorbance		Amount Recovered in µg		% Lable claim	
		RIS	THP	A_1	A_2	RIS	THP	RIS	THP
1	117.8	3	2	0.498	0.708	2.97	1.99	99.2	99.5
2		3	2	0.500	0.707	2.98	1.98	99.6	99.16
3		6	4	0.545	0.772	5.96	3.98	99.4	99.7
4		6	4	0.541	0.770	5.92	3.97	98.78	99.31
5		9	6	0.590	0.835	8.93	5.91	99.31	98.6
6		9	6	0.588	0.836	8.91	5.95	99.04	99.2
						Mean		99.22	99.24
						± S.D.		0.286	0.374
						C.V.		0.289	0.377

Table 3: Summary of result of Ruggedness studies

Parameter	Statistical data	Absorption correction method	
		RIS	THP
Interday	Mean	99.15	99.88
	± S.D.	0.409	0.660
	C.V.	0.412	0.661
Intraday	Mean	99.13	99.93
	± S.D.	0.472	0.611
	C.V.	0.476	0.611
Different analyst	Mean	99.54	98.93
	± S.D.	0.585	0.450
	C.V.	0.588	0.455

RESULTS AND DISCUSSION:

An attempt has been made to develop a fast, sensitive, precise, reproducible and economical analytical method for simultaneous estimation of RIS and THP in their combined dosage form. In this method RIS and THP obey Beer's law in the concentration range of 0 to 40 µg/ml and 0 to 80 µg/ml. It was observed that both the drugs showed additivity of absorbance at selected wavelengths indicating that both the drugs do not interact with each other in the solvent system used. A (1%, 1cm) values were also calculated for both the drugs. For THP, A (1%, 1cm) was found to be 76.3 at wavelength 219 nm and for RIS, it was 165.1 and 161.3 at wavelength 282 nm and 219 nm respectively. The result of percentage estimation of drug is shown in Table1. The method was validated as per the ICH and USP guidelines. The results of recovery study were found to be within the prescribed limit of 98 - 102 %, proving the accuracy and showing that the method is free from interference from excipients. The results are shown in Table 2. For precision, replicate estimation of both RIS and THP in the same batch of tablets was done by proposed method, which yielded quite concurrent results, indicating reliability of the method. The values of SD or RSD are within the prescribed limit of 2 %, showing high precision of the method, as shown in Table 1. For ruggedness the proposed method was repeated under different conditions like different time, on different day and by different analyst. The results shown in Table 3 prove that the method is reproducible. During the linearity study it was observed that absorbance values of RIS and THP in the marketed formulation were linear in the range of 80 % to 120 % of the test concentration with R^2 close to one for this method of analysis. From the study of validation parameters namely accuracy, precision (SD and RSD), ruggedness (interday, intraday and different analyst), linearity and range, it was observed that the method is specific, accurate, precise, reproducible and rugged. Hence, this method can be employed for routine analysis of tablet dosage form.

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