Spectrophotometric Estimation of Raltegravir Potassium in Tablets

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Ultra violet spectrophotometric estimation of the raltegravir potassium, an integrase inhibitor antiretroviral agent was estimated by Ultra violet absorption maxima method at λ_{max} of 328 nm and UV area under curve method in the wave length range of 323-333 nm. The Beer's law obeyed in the concentration range of 3-55 μg/ml and correlation coefficients were found to be more than 0.996 for both methods. The results of the analysis were 100.58±0.99 and 99.69±0.59 by absorption maxima and area under curve method respectively. Both the methods were validated as per ICH guidelines.

Keywords: UV spectrophotometry, raltegravir potassium, area under curve

Raltegravir, is a HIV integrase strand transfer inhibitor, which prevents the insertion of viral DNA into the genome of the hostcell and consequently viral replication. Raltegravir potassium, chemically potassium 4-[(4-fluorobenzyl)carbamoyl]-1-methyl-2-(1-methyl-1-{[(5-methyl-1,3,4-oxadiazol-2-yl)carbonyl] amino}ethyl]-6-oxo-1,6-dihydropyrimidine-5-olate[1]

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(fig. 1). Literature survey revealed that UV[2] and HPLC[2-5] methods were reported for the estimation of raltegravir potassium alone and in combinations with other drugs.In the reported UV method[2], the determination was carried out at λ_{max}219 nm by calibration curve method only with the linearity of 3-15 µg/ml in methanol. Hence, it was thought to determine raltegravir potassium by different UV methods to improve the analytical profile and linearity rangein UV methods.

All the chemicals of analytical grade were used. Spectral and absorbance measurement were made on a Shimadzu double beam UV/Vis spectrophotometer 1800 and a Systronic double beam UV/Vis spectrophotometer 2203 with 10 mm paired quartz cells. A Shimadzu balance (BL-220H) was used for weighing. Raltegravir potassium was obtained from Emcure Pharmaceuticals, Pune. The raltegravir potassium tablet, Isentress (Label claim 400 mg) of E. Merck (India) Ltd., Mumbai, were obtained from a local pharmacy shop.

A stock solution of raltegravir potassium (1 mg/ml) was prepared by dissolving 100 mg of raltegravirin a 50:50 mixture of methanol and water in a 100 ml volumetric flask. From the working standard solution, suitable dilutions (3-55 µg/ml) were obtained for linearity study.

In UV absorption maxima method, a solution of 10 µg/ml was scanned over the UV range, which gave the maximum absorbance at the wavelength. The $\lambda_{max}$of 328 nm was selected. Similarly, by using the same solution, the area under curve range was determined and found to be 323-333 nm (fig. 2). Both the methods were found to be specific as there was no change in the λ_{max} and absorbance of raltegravir potassium in the presence of the excipients. The linearity was found to be 3-55 µg/ml by both methods. Both the methods were validated as per ICH guidelines[6] for accuracy, precision, repeatability, limit of detection, limit of quantitation and ruggedness (Table 1).

Accuracy of the method was checked by recovery study using standard addition method at three different concentration levels (80, 100 and 120%). The recovery study results were found to be 99.36 to 102.31 with %RSD less than 2 (Table 2). The same solutions of recovery study were further evaluated on same day at three different times and on three different days for intraday and interday precision

TABLE 1: STATISTICAL PARAMETERS OF UV SPECTROSCOPIC METHODS

Parameters	Absorption maxima method	Area under curve method
Beer's law range	3-55 µg/ml	3-55 µg/ml
Coefficient of correlation (r^2)	0.996	0.999
Slope (m)	0.036	0.015
Intercept (c)	0.06	0.00
LOD (µg/ml)	0.91	1.18
LOQ (µg/ml)	2.77	3.60

LOD: Limit of detection, LOQ: limit of quantification, UV: ultraviolet

TABLE 2: RECOVERY STUDY OF UV SPECTROSCOPIC METHODS FOR DETERMINATION OF RALTEGRAVIR POTASSIUM

Recovery study (%)	Label claim mg/tab	Amount of substance added	Recovery±RSD* (%)	
			Absorption maxima method	Area under curve method
80	400	320	99.36±0.100	99.23±0.250
100	400	400	100.21±0.990	98.47±0.720
120	400	448	102.31±0.960	101.12±0.860

*n=3, RSD: relative standard deviation

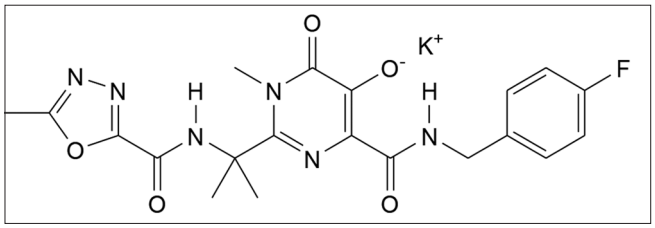

Fig. 1: Raltegravir potassium.

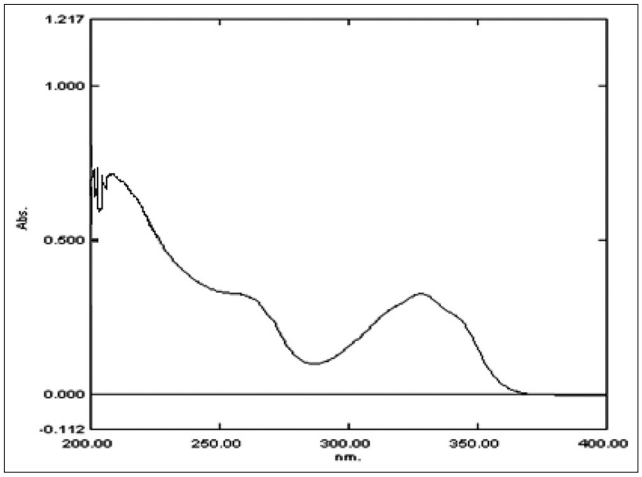

Fig. 2: UV spectrum of raltegravir potassium.
UV spectrum of raltegravir potassium was taken in a solution in methanol:water (50:50).

TABLE 3: RUGGEDNESS STUDY OF UV SPECTROSCOPIC METHODS FOR DETERMINATION OF RALTEGRAVIR POTASSIUM

Type of analysis	% estimated ± % RSD*	
	Absorption maxima method	Area under curve method
Analyst-1	100.58±0.990	99.69±0.590
Analyst-2	99.42±0.588	98.97±0.101
Instrument-1	100.96±0.993	100.15±0.998
Instrument-2	98.36±0.968	98.06±0.100

*n=5, RSD: relative standard deviation

TABLE 4: ROBUSTNESS STUDY OF UV SPECTROSCOPIC METHODS FOR DETERMINATION OF RALTEGRAVIR POTASSIUM

Parameter		Estimated±RSD* (%)	
		Absorption maxima method	Area under curve method
Methanol: Water	47.5:52.5	99.65±0.980	98.55±0.583
Composition (±5%)	50:50	100.25±0.986	99.23±0.587
	52.5:47.5	99.03±0.585	98.01±0.100
Wavelength (±5 nm)	323	101.55±0.210	100.05±0.997
	328	100.36±0.987	99.96±0.996
	333	101.88±0.990	101.80±0.880

*n=5, RSD: relative standard deviation

TABLE 5: RESULT OF ANALYSIS FOR RALTEGRAVIR POTASSIUM IN TABLET FORMULATION

Methods	Label claim mg/tab	Estimated* (%)	RSD* (%)
Absorption maxima	400	100.58	0.990
Area under curve	400	99.69	0.590

*n=5, RSD: relative standard deviation

study. The precision of both methods was found to be good with %RSD less than 2 (Table 2).

The limit of detection for raltegravir potassium were found to be 0.91 and 1.18 µg/ml for absorption maxima and area under curve method where as limit of quantification was found to be 2.77 and 3.60 µg/ml calculated for absorption maxima and area under curve method, respectively. The ruggedness of both the methods was performed by changing analysts and instruments. The results are given in Table 3. The robustness was performed by changing solution composition and wave length for both methods (Table 4).

Twenty tablets were weighed and powdered. Tablet powder equivalent to 100 mg of raltegravir potassium was accurately weighed and transferred into a 100 ml volumetric flask and to this 25 ml of methanol and water (50:50) was added. The solution was sonicated for 20 min and filtered through Whatman filter paper 41. The final volume was made up to 100 ml to obtain concentration of 1 mg/ml raltegravir potassium. This solution was further diluted to obtain concentration 10 µg/ml and was used in analysis. The results of analysis of tablet formulation were found to be 100.58±0.99 and 99.69±0.59 by absorption maxima and area under curve method respectively (Table 5).

Proposed two methods were simple, economical and reliable. In the reported methods linearity range was narrow i.e. 3-15 µg/ml whereas in the proposed methods the linearity was found in the range of 3-55 µg/ml. The methods are validated and can be used for routine analysis of raltegravir potassium in bulk and tablet dosage form.

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