Review on "Method Development and Validation by UV Spectroscopy for Estimation of apremilast formulation"

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Abstract

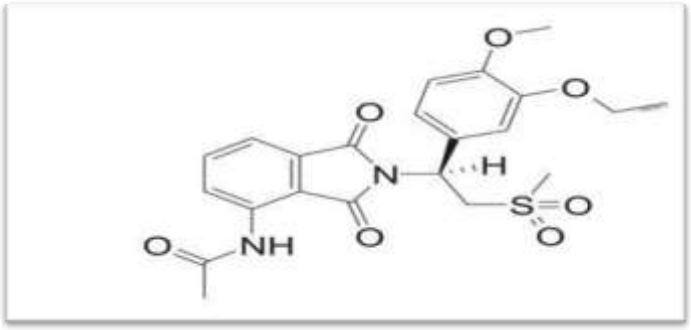
Apremilast is used for treatment of psoriasis and psoriatic arthritis. It may also be beneficial for other inflammatory diseases relevant to the immune system. The drug functions as a selective enzyme phosphodiesterase 4 (PDE4) inhibitor and avoids the spontaneous development of TNF-alpha from human synovial rheumatoid cells. The present review assesses the different approaches for evaluation of apremilast in bulk material as well as different formulations. A concise review consists of compile and discuss about over 30 methods for analyzing apremilast in the biological matrices, the samples of marketed and in different dosage formulations including UV-spectrophotometry.

Keyword: *Apremilast, Method development, UV spectroscopy, Forced degradation.*

Introduction:

Chemically, Apremilast is known as N-[2-[(1S)-1-(3-ethoxy4methoxyphenyl)-2(methylsulfonyl) ethyl]-1,3-dioxo2,3dihydro-1H-isoindol-4-yl] acetamide. It has a C22H24N207S and a molecular weight of 460.5g mole. (1). Apremilast is a drug approved by the Food and Drug Administration, used for psoriasis and psoriatic arthritis treatment. It may also be beneficial for other inflammatory diseases related to the immune system. The drug functions as a potent phosphodiesterase 4 (PDE4) enzyme inhibitor and prevents the spontaneous development of TNF-alpha. Apremilast is Phthalimide derivative. It is a white to pale yellow, non- hygroscopic powder that is virtually insoluble at a wide range of pH in water and buffer solutions but is soluble in lipophilic solvents including acetonitrile, butanone, acetone, dichloromethane, and tetrahydrofuran. It is manufactured in India by Glenmark Pharmaceutical, under the brand name Otezla and Aprezo. DSC, TGA, DVS and particle size distribution, as well as polymorphism system (characterized by XRPD, DSC, TGA, DVS, TGA/FT-IR and microscopic testing) Apremilast shows stereoisomerism due to the presence of a single chiral center, with the pharmacologically active (S)-enantiomer. Effective drug stability tests and clinical studies have shown that Apremilast (S)-enantiomer is not interconverted to its (R)enantiomer both on storage and in vivo. Polymorphism and seven polymorphic forms were observed for Apremilast (designated A-G) was named for the active substance. The desirable type B was found to be the most anhydrous form of Apremilast which is thermodynamically stable. The Production cycle consistently yields single crystal type B active substance.

A through literature survey reveals that not many analytical methods published to describe the quantification of Apremilast by UV-Spectrophotometric method7, RP-HPLC8,9 and UPLC Infect the published UV method utilizes methanol as solvent. But there is no stability indicating UV method with acetonitrile solvent. These stability indicating methods would be helpful in establishing the stability data of these drugs in bulk and tablet dosage forms. Generally, this UV technique is less expensive and with inherent simplicity. Rapid development in the pharmaceutical industries, producing a greater number of new drugs and formulations in different parts of world has been increasing. For providing effective and safe drug formulation to consumers direly needed. So
innovative new analytical methods necessary for controlling their quality and amount of drug in pharmaceutical dosage forms especially it plays a vital role in the case of powerful drugs.



Structure of Aprimilast

Qualitative analysis: **-** Qualitative analysis deals with the identification of element, ions or compound present in the sample.

Quantitative analysis: - Quantitative analysis deals with the determination of how much amount of one or more constituents present in sample.

Table no- 1. Drug Profile

Drug Name	Aprimilast
Category	Phoshodiesterase4(PDE4). Immunomodulating agent.
Chemical formula	C22H24N2O7S
IUPAC Name	N-[2-[(1S)-1-(3ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-1,3dioxoisoindol-4-yl]acetamide
Molecular weight	460.501 g/mol
Melting point	156-158°C
Solubility	Slightly soluble in water, sparingly soluble in Acetonitrile and Methanol.
Half-life	6 - 9 hours
Pak value Strongest acid-	Strongest acid-14.42 Strongest base- 8.91
log P value log P log P	log P 2.69 log P 2.74
L log S value	-3.1

Mechanism of action: -

UV- visible spectrophotometric method:

UV-Visible spectrophotometry is mostly used method in pharmaceutical research. This means calculating how much ultraviolet or visible radiation a material absorbs in solution. Ultraviolet-Visible spectrophotometers are the instruments that compute the correlation or function of the correlation of the intensity of two light beams in the UV-Visible region. Using a spectrophotometer, organic compounds can be detected in qualitative analysis, if any reported data are available, and significant spectrophotometric examination is used to determine the number of molecular species absorbing the radiation. Spectrophotometric technique is simple, fast, relatively precise, and applicable to small compound quantities. The Beer-Lambert law is the fundamental law governing quantitative spectrophotometric analysis.

Table. No-2: Regions of electromagnetic

Sr. No	Drug	Matrix	Method	Solvent	Detection	Linearity/ LOD, LOQ	Ref.
1.	Apremilast	Tablet	A double beam UVvisible spectrophotometer	Methanol	230nm	Linearity:2-10 µg/mL R2:0.999 LOD: 0.157µg/mL LOQ: 0.476µg/mL	12

2.	Aprimilast	Tablet	A double beam UV 1900 Pharm Aspe	Methanol	230nm	Linearity: 4-12µg/mL R 2: Method A (0.9988) Method B: (0.992)	7
3.	Aprimilast	Tablet		Methanol	230nm	Linearity: 20-100µg/ml R2: 0.999 LOD: 0.157µg/mL LOQ: 0.476µg/mL	15

Beer's law: It states that the intensity of a parallel monochromatic radiation beam decreases exponentially with the numb er of molecules that are absorbed. To put it another way, abs orbance is proportionate to concentration.

Lambert's law: It states that the frequency of a parallel mono chromatic radiation beam diminishes exponentially as it travels through a homogeneous thickness medium. Combining these two laws gives rise to the Beer-Lambert law.

Beer-Lambert law:

If light beam is passed through a translucent cell containing an absorbing compound solution, there may be a decrease in light intensity. The Beer Lambert Law is ex pressed in mathematical terms as

A = a b c

Where,

A = absorbance or optical density

a = absorptivity or extinction coefficient

b = path length of radiation through sample (cm)

c = concentration of solute in solution.

Both b and a are constant so a is directly proportional to the concentration.

Table No.3: UV-Spectroscopy Method for Aprimilast

Region	Wavelength
Far (or vacuum) ultraviolet	10-200 nm
Near ultraviolet	200-400 nm
Near infrared	0.75- 2.2 µm
Mid infrared	2.5-50
Far infrared	50-1000 µm

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Preparation of Calibration curve:

A calibration curve was plotted over a concentration range of 10-40 µg/mL for Apremilast. Precisely measured standard solution of Apremilast (1,2,3, and 4 mL) was shifted to a series of 10 milliliter volumetric flasks and the volume was filled up to 10 mL with acetonitrile. Calibration curve

was done by plotting Apremilast concentration on X-axis and their respective absorbance's on Y-axis.

Calibration data is shown in Table 1. The optical characteristics are reported in Table 3. Figure 2 shows

the overlain spectrum

TableNo.4: Calibration Data of Aprimilast

Sr no.	**Concentration** (mcg/ ml)	**Peak area***
1.	10ppm	0.434
2.	20ppm	0.812
3.	30ppm	1.231

4.	40ppm	1.612

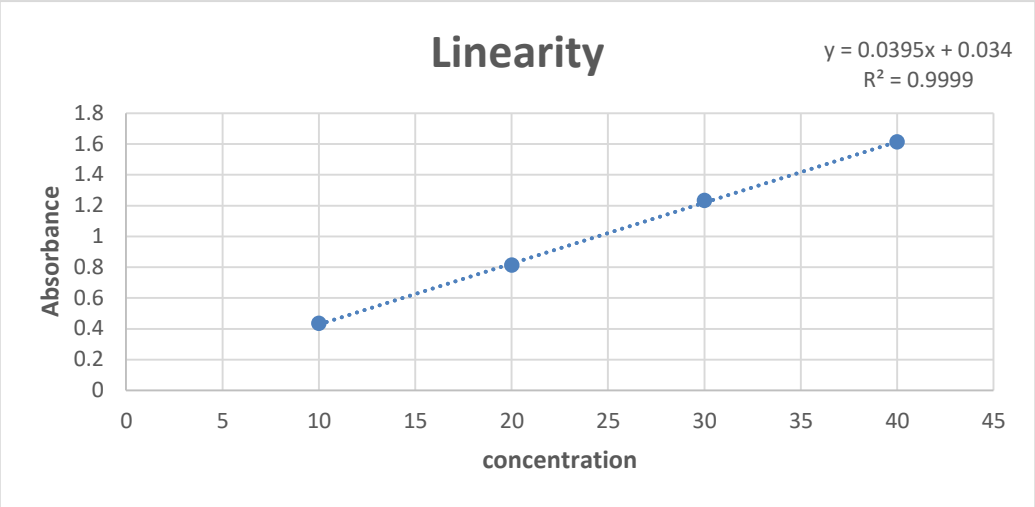
Linearity: -

Definition- which linearity is a mathematical relationship between two variables Quantities are directly proportional to each other.

y = mx + b.

y = 0.1303x+0.0026

linearity



(r2=0.9999)

Regression Equation	Y= 0.0395x5+0.034
Correlation coefficient	0.9996
Slope	0.0395
Intercept	0.034

Accuracy:

The ability of a measurement to match the actual true value of the quantity being measured. The expected ability for a system to discriminate between two setting. Smaller the bias more accurate the data.

Table no: -5

Level	Volume of solution A	Volume of solution B		Abs	Mean	SD of conc.	%RSD
80%	1	0.8	Make up the volume up to 10 ml	0.422	0.562	0.126	97.2%
	1	0.8		0.537			
	1	0.8		0.729			
100%	1	1		0.730	0.642	0.137	92.3%
	1	1		0.540			
	1	1		0.656			
120%	1	1.2		0.624	0.769	0.112	98.2%
	1	1.2		0.729			
	1	1.2		0.956			

Precision:

The precision of an instrument indicates its ability to reproduce a certain reading with a given accuracy OR it is the degree of agreement between repeated result.

Table no: -6

Sr.no	Volume of solution B		Conc X (ug/ml)	Abs	Abs after day	Intra day
1	1	Make up to volume up to 10 ml	10	0.729	0.729	0.730
2	1		10	0.690	0.695	0.693
3	1		10	0.746	0.744	0.749
4	1		10	0.820	0.822	0.823
5	1		10	0.730	0.731	0.730
6	1		10	0.576	0.610	0.620

LOD and LOQ:

Limit of Detection and Limit of Quantitation were calculated using following formula LOD = 3.3*(SD) / S and LOQ = 10 *(SD) / S, where SD = standard deviation of absorbance and S = slope of

Table no: -7

Parameter	Results
Limit of Detection (LOD)	0.157 µm/ml
Limit of Quantitation (LOQ)	0.476 µm/ml

the calibration. The results of LOD and LOQ are shown

Procedure for assay of pharmaceutical formulations:

Twenty Apremilast (Apxenta) marketed tablets were accurately weighed, finely powdered and average weight of each tablet was determined and the tablet fine powder equivalent to 10 mg of Apremilast was taken into hundred milliliter graduated flask and dissolved in ACN (methanol) to get 100 µg/mL concentrations. The solution was then sonicated for 20 min and filtered & further dilutions were done with ACN to get eventual concentration (10 µg/mL) within the linearity range and measured ʒmax at 22λ.3 nm. Finally, the drug content in each tablet and also bulk drug was found by utilizing the standard graph.

For analysis of bulk drug:

10 mg of bulk drug accurately weighed in 10 mL of measuring flask, 3 mL of ACN was added to get the drug soluble and eventually the volume was filled up to 10 mL by
utilizing ACN and required concentration ((10 µg/mL) was prepared and determined the absorbance. Table shows the assay results of pharmaceutical formulation (Apxenta) and bulk drug.

There were no UV methods have been reported (with acetonitrile as solvent) so for the determination of Apremilast in bulk as well as pharmaceutical tablet. None of the usual excipients employed in the formulation of Apremilast dosage forms interfered in the analysis of Apremilast by the developed method. Validation parameters are found within the limits. Infect, the magnitude of degradation was in the order of Alkaline> Acidic> Photolytic > Oxidative> UV light> Thermal. It was observed that all the statistical analysis results of % RSD values particularly precision, accuracy are observed below two which speaks that the method is precise and accurate. The results of pharmaceutical formulations assert that the proposed method of Apremilast aptly feasible for their determination without interfering the additives and excipients. Therefore, this method was simple, precise, accurate and cost effective and in actual fact feasible for routine sample analysis of Apremilast in bulk and pharmaceutical tablets

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