Method Devlopment of Apremilast (API) in Methanol by UV-Visible Spectroscopy

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ABSTRACT

A simple, precise, accurate, cost effective stability indicating UV Spectrophotometric method has been developed for the estimation of Apremilast. Apremilast shows highest λmax at 340 nm. Beer's law (linearity response) was found over a concentration range of 10-60 μg /mL with good correlation coefficient (r2 = 0.9994). The Proposed spectrophotometric method was validated as per the ICH Q1A (R2) guidelines. Hence this method can be safely be employed for the routine quality control analysis of Apremilast.

Keywords: Apremilast, Method Development, uv-visible spectroscopy

INTRODUCTION

The chemical name of apremilast is N-[2-[(1S)-1-(3-ethoxy-4- methoxyphenyl)-2-(methylsulfonyl)ethyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-4-yl]acetamide
and it is a drug for the treatment of certain types of psoriasis and psoriatic arthritis. It may also be useful for other immune system related inflammatory diseases. The drug acts as a selective inhibitor of the enzyme phosphodiesterase 4 and inhibits spontaneous production of tumor necrosis factor-alpha from human rheumatoid synovial cells

Apremilast was approved by the United States Food and Drug Administration (US-FDA) in March 2014 for the treatment of adults with active psoriatic arthritis. Apremilast is the first oral agent that is FDA-approved for the treatment of psoriatic arthritis and offers the convenience of oral dosing compared to treatment with biopharmaceuticals. In September 2014, the US-FDA approved apremilast for the treatment of moderate to severe plaque psoriasis. It is also being tested for its efficacy in treating other chronic inflammatory diseases such as ankylosing spondylitis, Behcet's disease, and rheumatoid arthritis

Apremilast is a white to pale yellow non-hygroscopic powder with a melting point range of approximately 150-152°C. It is practically insoluble in water, slightly soluble in ethanol, and soluble in , methanol, acetone. Apremilast is the S-enantiomer with a specific rotation of +28.1° in acetonitrile at a concentration of 20 mg/mL [5].
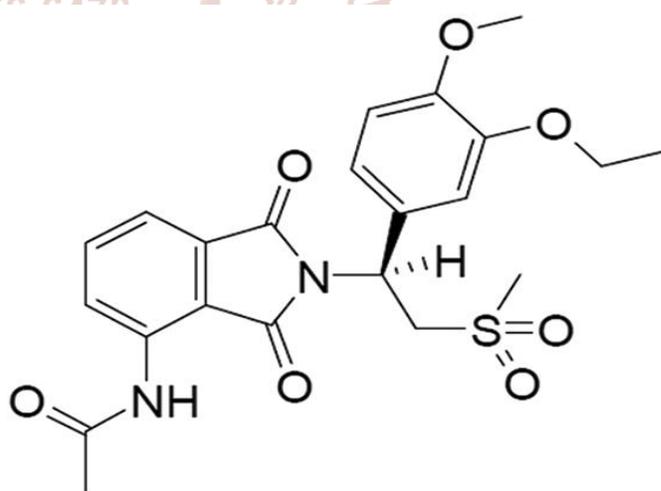
Apremilast structure is shown in Fig. 2.

Fig:-2

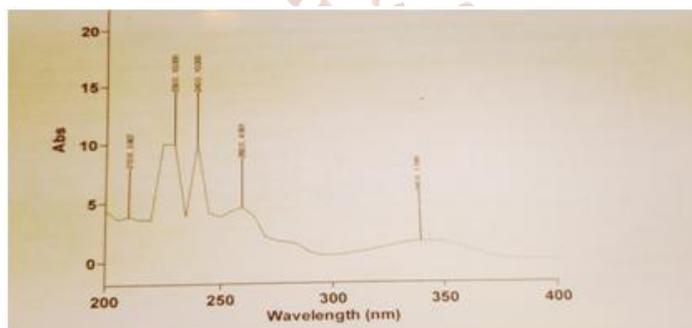**Melting point:** 150-152 ºC

MATERIALS AND METHODS

Materials:

Apremilast pure drug was procured as gift sample by Mankind Research Centre,Gurgaon Haryana, India. Methanol was procured from the CDH Delhi.

Selection of solvent:

Copious trails were done to find out the right solvent system for dissolving the drug. The solvents like acetonitrile, methanol, Ethanol, Chloroform, distilled water, different phosphate buffer of different pH and dimethyl sulfoxide [DMSO] were tried depending on the solubility of the Apremilast. Apremilast is soluble in organic solvents such as acetonitrile,Methanol,Ethanol and DMSO. Insoluble in distilled water and phosphate buffer of different pH . Based on the solubility Methanol was selected all the way through the experiment.

Selection of detection wavelength:-

To determine the optimum λmax, Apremilast 10 µg /mL of working standard solution was prepared and scanned in UV wavelength range of 200 - 400 nm utilizing as a blank. It was observed methanol that the drug showed maximum absorbance at 340nm which was chosen as the detection wavelength for the estimation of Apremilast.

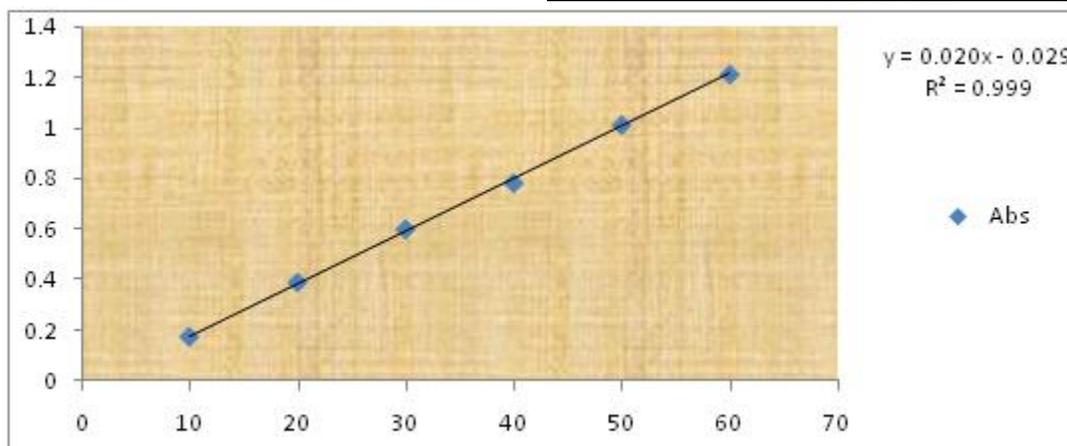### Preparation of stock and working standard solution:

Apremilast 10 µg/ mL standard stock solution was done by transferring precisely weighed 10 mg of standard Apremilast to 10 ml volumetric flask and dissolved in methanol. The volume was filled up to the mark with methanol. From this solution 1 ml was precisely transferred into 100 ml volumetric flask and volume was made up to the mark with methanol. Working standard solutions of Apremilast was prepared by suitable dilution of the stock solution (10 µg/mL) with the methanol.

Preparation of Calibration curve:

A calibration curve was plotted over a concentration range of 10-60 µg/mL for Apremilast. Precisely measured standard solution of Apremilast (1,2, 3, 4, 5, and 6 mL) was shifted to a series of 10 ml volumetric flasks and the volume was filled up to 10 mL with methanol. 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 of Apremilast. The calibration curve is exhibit in Figure 3.

Trial:-1

Concentration (µg/ml)	Absorbance
10	0.1740
20	0.3898
30	0.6004
40	0.7828
50	1.0131
60	1.2139

$y = 0.020x - 0.029$
$R^2 = 0.999$

DISCUSSION:

The UV spectra of Apremilast were scanned in the region between 200-400 nm. Apremilast show absorbed maximum at 340nm which was selected as the detection wavelength. The response of the Apremilast was found to be linear in the ranges from 10-60 µg/mL with a good correlation.

CONCLUSION

Simple, precise and economical UV-visible spectrophotometric method has been developed for the quantitative estimation of Apremilast in its API form. Method is devloped as per the ICH guidelines. The developed method can be used for the quantification of Apremilast drug substances in routine analysis.

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