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An Overview on Analysis of Apremilast

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ABSTRACT
Apremilast is an anti-inflammatory drug. The plethora subscribed in this work is directed towards the collection of various important methods used for the estimation of Apremilast from its bulk and formulations. As the newer guidelines from ICH had been directed towards the qualitative estimation of drugs from its bulk and formulations are made significant as it directly related towards the effectiveness of the drugs.
Key-words: Apremilast, Method development, analysis, validation

I. INTRODUCTION

Apremilast, also known as Otezla, is a phosphodiesterase 4 (PDE4) inhibitor used to treat various types of symptoms resulting from certain inflammatory autoimmune diseases. It belongs to the same drug class as Roflumilast and Crisaborole. Initially approved in 2014, it is marketed by Celgene. In July 2019, apremilast was granted a new FDA approval for the treatment of oral ulcers associated with Behcet's disease, an autoimmune condition that causes recurrent skin, blood vessel, and central nervous system inflammation. [1]

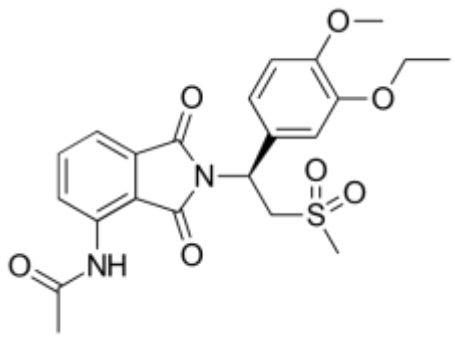

Fig. No. 01: Structure of Apremilast

II. METHODS USED FOR ANALYSIS OF APREMILAST

[1] Badhe P et al in the year **2019** had been reported with Badhe P et al in the year **2019** had been reported with A selective method for separation and determination of potential related impurities (starting materials and by-products of synthesis, and degradants) of apremilast drug substance has been developed and validated. The separation was accomplished on a Cosmosil C-18 (250 mm × 4.6 mm, 5 µm) column connected to a photodiode array (PDA) detector using optimized mixture of 0.05% trifluoroacetic acid, methanol and acetonitrile under gradient elution. Two major degradant impurities found in force degradation study of apremilast drug substance. Both degradants were characterized preliminarily by HPLC-MS studies and synthesized in laboratory. Structure was evidenced by NMR spectroscopy, mass spectrometry and HPLC method was developed for quantification of the synthesized impurities along with starting materials. This method can be used for the quality control testing of drug substance. The performance of the method was validated according to the ICH guide lines for specificity, limit of detection, limit of quantification, linearity, accuracy, precision, ruggedness and robustness.[2]

[2] Rina Mohan Sonawane et al in the year **2019** had been reported with reverse phase high performance liquid chromatographic method for analysis of Apremilast, as bulk drug. Apremilast is used to treat psoriatic arthritis. The separation was achieved by using a mobile phase of Methanol: Water (80:20, v/v) on a Grace C18 column (250mm x 4.6ID, 5µm) at flow rate of 0.8 ml/min. The detection was done at 231 nm. The retention time of Apremilast was 4.80 minutes. Calibration plot was linear (r2=0.9998) over a range of 2-5µg/ml. The method was validated for linearity, accuracy, precision, robustness and recovery. The proposed method was successfully used for quantitative determination of Apremilast. The high recovery and low relative standard deviation confirm the suitability of the method for

routine determination of Apremilast in tablet dosage form.[3]

[3] Hemaraj R. Patil, et al in the year **2019** had been reported with. The HPLC Method for Apremilast was developed using Cosmosil C18 (4.6mm x 250mm, Particle size: 5µm), as stationary particle, isocratic mode. Methanol: Water (80:20v/v) pH3 as mobile phase. Mobile phase was maintained at a flow rate of 0.8 ml/min and detection was carried out at 230 nm. Both the methods were validated in accordance with ICH guidelines[4]

[4] Chaudhari SR, et al in the year **2019** had been reported with Optimized experimental conditions for proposed work consists of methanol and water, pH 3.50 adjusted with ortho-phosphoric acid (70:30 % v/v) as a mobile phase at a flow rate 1 ml/min with a retention time was found to be 5.15 min. Accuracy study was completed at three different levels and was found in the range of 99.44–101.49%.[5]

[5] Landge SB, et al in the year **2017** had been reported with A new, specific, rapid and stability indicating reversed phase liquid chromatographic (RP-LC) method for the determination of process related and degradation related impurities of Apremilast has been developed and validated. The degradation study performed in acid, base, oxidative, photolytic, and thermal stressed conditions. Eight process related impurities (Imp-1 to Imp-8) in test sample of Apremilast have been detected by developed RP-LC method. The good chromatographic resolution between the peaks of process related impurities, degradation impurities and Apremilast has been achieved on a Synergi Max-RP 80 A (150 × 4.6 mm ID), 4 µ column. The process and degradation related impurities were characterized by mass spectrometry, 1H NMR and FT-IR spectral data. The method was validated as per ICH guideline and found to be specific, rapid, and stability indicating. The proposed RP-PLC method was successfully applied to the analysis of drug substance samples of Apremilast.[6]

[6] Chaudhari SR, et al in the year **2018** had been reported with Apremilast is small molecule inhibitor of phosphodiesterase-4 (PDE-4) and an immunomodulating agent which is used for management of refractory psoriatic arthritis. Material and Methods: HighPerformance Thin-Layer Chromatography (HPTLC) method for the analysis of apremilast was developed and validated as per ICH guidelines. Apremilast was chromatographed on silica gel 60 F254 TLC plates using toluene: methanol (8:2 v/v) as a mobile phase. A Compact spot for apremilast was observed with Rf 0.64 ± 0.05, when the densitometric scanning was implemented at 230 nm. The linear regression analysis data for the calibration plots showed r2 > 0.99 with a concentration range from 250 – 1500 ng/band. 'Design of Experiments' (DoE) employing 'Box-Behnken Design' (BBD) and 'Response Surface Methodology' (RSM) were studied as an advancement to traditional 'One Variable at Time' (OVAT) approach to assess the effects of variations in selected factors particularly (development distance, saturation time, activation time of plate and mobile phase ratio) as graphical interpretation for robustness. The statistical insight was achieved with Multiple Linear Regression (MLR) and ANOVA. Results: The method was validated for precision, accuracy, detection limit and quantitation limit, and robustness. Conclusion: The method was successfully employed for the determination of apremilast from its in-house tablet formulation.[7]

[7] Chakravarthy AV et al in the year **2017** had been reported with Method development and validation of ultraviolet-visible spectroscopic method for the estimation of assay of sugammadex sodium, Apremilast, riociguat, and vorapaxar sulfate drugs in active pharmaceutical ingredient form [8]

[8] Intwala JK, et al in the year **2017** had been reported with Development And Validation Of Sophisticated Analytical Method For The Estimation Of Apremilast [9]

[9] Hemaraj R. Patil et al in the year **2019** had been reported with Devlopment And Validation of Uv-Spectrophotometric and Hplc Method for Apremilast In Bulk and Tablet Dosage Form [10]

[10] Lonkar NA, et al in the year **2017** had been reported with Development and validation of UV spectrophotometric method for the estimation of apremilast in bulk form by absorbance maxima method. [11]

[11] Chaudhari SR, et al in the year **2019** had been reported with Design of experiment avenue for development and validation of RP-HPLC-PDA method for determination of apremilast in bulk and in in-house tablet formulation. [12]

[12] Landge SB, et al in the year **2017** had been reported with Development and validation of

stability indicating rapid RP-LC method for determination of process and degradation related impurities of Apremilast, an antiinflammatory drug. [13]

[13] Chaudhari SR, et al in the year **2018** had been reported with Application of Box-Behnken Design for Validation of High Performance Thin-Layer Chromatography/Densitometry Method for Robustness Determination of Apremilast in Bulk and inhouse Tablets. [14]

[14] Chakravarthy AV et al in the year **2017** had been reported with Method development and validation of ultraviolet-visible spectroscopic method for the estimation of assay of sugammadex sodium, Apremilast, riociguat, and vorapaxar sulfate drugs in active pharmaceutical ingredient form [15]

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[17] Lonkar NA, et al in the year **2017** had been reported with Development and validation of UV spectrophotometric method for the estimation of apremilast in bulk form by absorbance maxima method. [18]

[18] Chen LG, et al in the year **2016** had been reported with Determination of apremilast in rat plasma by UPLC–MS-MS and its application to a pharmacokinetic study [19]

[19] Lonkar, N. et al in the year **2017** had been reported with Development and Validation of Stability Indicating RP-HPLC Method for The Estimation of Apremilast By Forced Degradation Studies [20]

[20] Rajan V Rele et al in the year **2018** had been reported with Reversed Phase High Performance Liquid Chromatography Method for Determination of Assay and Forced Degradation Study Of Apremilast From Active Pharmaceutical Dosage Form [21]

[21] Ravisankar P et al in the year **2017** had been reported with Development and validation of stability-indicating UV spectrophotometric method for determination of Apremilast in bulk and pharmaceutical dosage form [22]

[22] Kulsum S, et al in the year **2016** had been reported with Method development and validation of forced degradation studies of apremilast by using UV spectrophotometric method [23]

III. CONCLUSION

The analytical chemist mainly directs his research towards the development and validation of analytical methods for the estimation of Drugs from its bulk and formulations. In the view of this fact here a details about the various methods used for the estimation of Apremilast form bulk and formulations had been studied expensively for its application in further research.

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