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Abstract of the Thesis

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Title of the Thesis: **STUDY ON DEGRADATION BEHAVIOR AND IMPURITY PROFILING OF BULK DRUGS AND THEIR FORMULATION OF SOME SELECTED ANTI-DIABETIC DRUGS**

Abstract

The research problem in impurity profiling of degradation impurities in anti-diabetic drugs centers around the need to accurately identify and quantify potentially harmful degradation products that may arise during the drug's shelf life. Anti-diabetic medications are critical for managing diabetes, and their efficacy and safety are paramount. However, these drugs can degrade over time due to environmental factors such as temperature, humidity, and light, leading to the formation of various impurities. These degradation impurities can impact the drug's therapeutic effectiveness and safety profile. The challenge lies in developing and validating robust analytical methodologies that can effectively detect and quantify these impurities at low concentrations, ensuring they remain within acceptable limits throughout the drug's shelf life. Additionally, understanding the degradation pathways and mechanisms is crucial for predicting impurity formation and mitigating potential risks. Addressing this research problem involves a comprehensive approach, including stress testing, advanced analytical techniques, regulatory compliance, and method validation, to safeguard the quality and efficacy of anti-diabetic drugs.

The methodology for impurity profiling of degradation impurities in anti-diabetic drugs involves a multi-faceted approach to ensure drug safety and efficacy. Initially, stress testing is conducted, exposing the drug to various conditions such as heat, humidity, light, oxidation, and hydrolysis to induce degradation and identify potential impurities. Analytical techniques are then employed to analyze these impurities, with Preparative High-Performance Liquid Chromatography (HPLC) being pivotal for separating and quantifying degradation products. Mass Spectrometry (MS) provides detailed identification and quantification of impurities based on their mass-to-charge ratios. Nuclear Magnetic Resonance (NMR) Spectroscopy offers structural insights into these degradation products, while Infrared Spectroscopy (IR) helps identify specific functional groups. Understanding the degradation pathways of the drug helps in predicting and controlling impurity formation. Finally, method validation is conducted to confirm that analytical methods are accurate, precise, specific, and sensitive, ensuring reliable and reproducible results. This thorough methodology ensures a robust evaluation of degradation impurities, supporting the drug's safety and therapeutic effectiveness.

A simple, precise, accurate, specific, linear, rugged and robust method was developed and validated for the estimation of degradation impurities of Empagliflozin and Dapagliflozin in API and tablet formulation. Chromatographic conditions were used as Stationary phase YMC ODS A C-18 (150mm x 4.6mm), Mobile phase Acetonitrile: Water in the ratio of 50:50 and flow rate was maintained at 0.5 ml/min and 0.7 ml/min, detection wave length was 224 nm and 273 nm for Empagliflozin and Dapagliflozin, respectively. Column temperature was set to 35ºC and diluent was mobile phase. Validation is performed according to ICH Guidelines Q2(R1).The degradation study of both the drugs under stressed conditions was examined following ICH guidelines Q1(R2).Empagliflozin and Dapagliflozin were subjected to oxidative, acidic, alkaline, neutral, photolytic, and thermolytic degradation conditions. The drug was stable in Oxidative, thermal, and photolytic conditions, and no degradation products were observed. For Empagliflozin two degradation products were formed in acid (DP-1,RT:2.28 min) and Alkali stress hydrolysis conditions (DP-2, RT:2.25 min) and for Dapagliflozin two degradation products formed in acid (DP-1,RT: 6.90 min) and Alkali stress hydrolysis conditions (DP-2, RT: 2.3 min). All the degradation Impurities are observed and well separated in same developed method. Unknown impurity formed during stability studies was isolated using preparative HPLC and structure was characterized by ^{1}H NMR, FTIR and Mass spectroscopy studies. Empagliflozin and Dapagliflozin with its tablet formulation is more sensitive towards acid and Alkali degradation.

Impurity profiling of anti-diabetic drugs is a critical process in pharmaceutical development that ensures the safety, efficacy, and quality of these medications. By identifying and quantifying impurities—unwanted chemicals that may be present in drug formulations—scientists can assess potential risks such as reduced therapeutic efficacy or adverse reactions. This profiling involves sophisticated analytical techniques like high-performance liquid chromatography (HPLC) and mass spectrometry to detect trace amounts of impurities and understand their origins. This comprehensive analysis helps in optimizing drug formulations, complying with regulatory standards, and ultimately ensuring that patients receive safe and effective anti-diabetic treatments.

This PhD thesis will be useful for enhancing the safety and efficacy of diabetes treatments by providing critical insights into degradation impurities and their impact. It will support pharmaceutical companies in developing more stable and effective formulations, aid regulatory bodies in ensuring drug quality standards, and offer researchers advanced methodologies for impurity detection and analysis.

Ultimately, it will contribute to better patient outcomes by ensuring that anti-diabetic drugs remain safe and effective throughout their shelf life.

List of Publication(s):

1) Dhara Vashi, Suresh kumar, Monika Kakadiya, "Structural characterization of Forced degradation impurity of Dapagliflozin ". Chinese Journal of Medical genetics, Vol. 32 Issue. 1(2023). pp-1006-1016. ISSN: 1003-9406.
2) Dhara Vashi and Suresh kumar, "Development and Validation of Stability indicating RP-HPLC method for estimation of Empagliflozin." World journal of pharmaceutical research "Vol. 13 Issue. 9 (2024). Pp-1538-1551. ISSN 2277-7105.
3) Dhara Vashi and Suresh kumar,"Impurity identification and Characterization some Anti-Diabetic drugs using of various analytical methods". Asian Journal of Pharmaceutical Research. Vol. 9 Issue. 4 (2019).pp-243-248. ISSN: 2231-5691