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PIOGLITAZONE'S PHOTOSTABILITY AND DEGRADATION DYNAMICS

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ABSTRACT

This research aims to explore the Pioglitazone which belongs to the thiazolidinedione-class drugs demonstrates broad usage in type 2 diabetes mellitus treatment through enhancement of insulin sensitivity. The pharmaceutical properties of Pioglitazone suffer major deterioration because of its high sensitivity to UV light exposure. This research examined pioglitazone hydrochloride photostability dynamics using different pH solutions (1.0–12.0) along with UV treatment. The degradation processes were monitored at 269 nm with spectrophotometry and analyzed for photodegradation products through HPLC. Laboratory data confirmed that pioglitazone degrades following first-order kinetics yet it shows peak stability when kept at pH 8.0 yet experiences maximum decay at pH 12.0. An additional testing phase in simulated gastrointestinal solutions confirmed stability of the drug substance under gastric acid but the drug substance experienced substantial degradation in alkaline solutions. Protective polymer matrices shield pharmaceutical materials from photodegradation effects while antioxidant addition of ascorbic acid further strengthens this protective scheme. The data confirms why proper pharmaceutical storage practices must include packaging solutions combined with pH management systems for protecting drug potency. Photostability testing remains vital for pharmaceutical development because the findings point toward future research opportunities which should focus on enhancing pioglitazone's stability by examining nanoparticle encapsulation alongside stabilizing agents.

Keywords: Pioglitazone, photostability, degradation kinetics, UV irridation, pharmaceutical stability

Introduction

The pharmaceutical drug Pioglitazone hydrochloride works as a PPAR-γ agonist to enhance insulin sensitivity in adipose tissue, muscle and liver cells through PPAR-γ agonism and thus it helps regulate glucose homeostasis (Satheeshkumar et al., 2014). The therapeutic success of pioglitazone hydrochloride strongly depends on its stability and especially on its resistance to light because photodegradation can lead to poisonous byproducts or impaired drug potency. The International Council for Harmonization (ICH) requires photostability assessments to determine the breakdown effects from UV radiation because studies demonstrate pioglitazone reacts quickly when exposed to light at basic pH levels (ICH, 2019; Ashour et al., 2015). Drug quality might become compromised through degradation so protective strategies must be identified to prevent this issue. Scientists investigate pioglitazone photostability by testing it under laboratory control settings which evaluate the breakdown patterns and stabilization processes through antioxidant additions and polymer-based containment systems for light decomposition reduction. Studies demonstrate that pH values determine drug breakdown rates while

revealing alkaline conditions as key factors which lead to structural changes yet current knowledge about protective methods remains insufficient. This study evaluates different kinetic models alongside stabilization methods because its main objective is to guide advanced formulation development which extends product shelf life and retains therapeutic properties. These stabilization methods will boost the stability of pioglitazone which would result in better clinical effects with enhanced patient protection and regulatory compliance. The research findings support the development of better pharmaceutical solutions for environmental factors that attack drugs and they establish protective methods for maintaining drug stability within diabetes treatment

Background On Pioglitazone

Pioglitazone hydrochloride stands as the lead medication belonging to the thiazolidinedione class which regulates type 2 diabetes mellitus (T2DM). The pharmacological activity of pioglitazone hydrochloride functions through PPAR-γ agonism to enhance insulin sensitivity in cells from different tissues including adipose tissue muscles and liver cells through insulin resistance reduction and hepatic glucose suppression and lipid metabolism optimization (Satheeshkumar et al., 2014). The stability system in pioglitazone leads to controlled blood sugar levels that experts prefer for both single-diabetic therapy and additional therapy in diabetes patients (Kalliokoski et al., 2008). The effectiveness of the treatment depends on preserving its chemical composition because exposure to light or elevated heat or pH conditions can damage its structure which may create unfavorable patient outcomes.

Importance Of Photostability

The ICH guidelines specify that testing for pioglitazone photosensitivity needs to determine damaging compounds which decrease drug efficiency or create hazardous substances. UV irradiation in basic solutions speeds medication degradation at the same time it produces dangerous substances that may reduce therapeutic effectiveness while protective barriers and antioxidants help stabilize drug formulations.

The drug product pioglitazone requires photostability assessment due to the following reasons:

Regulatory Compliance

The International Council for Harmonization through ICH (2019) specifies that pharmaceutical manufacturers need to test photostability because it detects degradation products that interfere with drug potency or create harmful compounds.

Safety And Efficacy Risks

The risks of degradation and reduced efficacy with pioglitazone occur because UV rays work faster when exposed to alkaline solutions (Ashour et al., 2015). Patient safety risks exist from degradation products because they can both modify therapeutic effectiveness and initiate toxic substances (Sharma et al., 2010).

Formulation Challenges

The formulation process faces challenges when light comes into contact with pioglitazone because it leads to instability which can be managed through the use of protective approaches including polymer coatings together with antioxidants (Patel & Singh, 2017).

Research Objectives

The research analyzes the pH-dependent UV breakdown (1.0–12.0) of pioglitazone by HPLC and spectrophotometry (269 nm) under simulated gastric conditions (pH 1.0) and intestinal conditions (pH 12.0) before creating stabilization approaches (HPMC polymer encapsulation and BHT/ascorbic acid antioxidants) that will guide production enhancements through pH management and nanoparticle delivery systems.

This study aims to:

Investigation Of Degradation Under Different PH

This research evaluates the degradation of pioglitazone when subjected to uv light at different pH levels (1.0–12.0 using spectrophotometric detection at 269 nm with HPLC testing for product degradation identification.

Evaluation Of Simulated Gastrointestinal Conditions's Stability

The drug stability evaluation includes testing the drug under simulated pH 1.0 gastric acid solution and pH 12.0 intestinal base.

Stabilization Strategies Development

i. The lab work must evaluate methods to protect the drug through:

ii. Polymer-based encapsulation: In order to shield against UV light, including the example of HPMC.

Antioxidant Additives

The incorporation of BHT with ascorbic acid serves to protect against growing reactive oxygen species.

Improvements In Formulation

The team can utilize their gathered data to establish recommendations regarding pioglitazone stability through pH regulation methods and better packaging innovations involving nanoparticle encapsulation technology.

Research Questions

a. The first-order decay characteristic of your analysis was proved by data showing $k = 0.0185\ h^{-1}$ at pH 12.0.

b. Adding HPMC with ascorbic acid resulted in a 58% reduction of degradation rates (Patel and Singh, 2017).

c. Per tests performed using simulated gastrointestinal conditions the medication remained stable at acidic pH 1.0 then quickly deteriorated at basic pH 12.0.

d. Two degradation products were tracked using HPLC but researchers have not investigated their toxicity characteristics (Rezk et al., 2012).

e. The proposed nanoparticle encapsulation method indicates new directions which should improve stability in accordance with ICH standards (ICH, 2019)

Hypothesis

a. Under UV irradiation Pioglitazone degrades according to first-order kinetics while its rates expand exponentially at pH values greater than ten through ring thiazolidinedione ring cleavage and hydrolysis mechanisms.

b. When hydroxypropyl methylcellulose (HPMC) encapsulation teams up with ascorbic acid at pH 12.0 it protects pioglitazone from UV exposure by more than 50% better than either approach used separately.

c. The stability of Pioglitazone matches its acidic pH 1.0 gastric segment yet shows rapid degradation at alkaline pH 12.0 intestinal fluid levels because of its pH-sensitive photodegradation characteristics.

d. The HPLC findings will detect two main degradation products which match ring-opened metabolites because they weaken PPAR-γ agonist activity.

Limitations

a. This investigation limited itself to laboratory-based photodegradation analysis while omitting examinations of drug behavior within human bodies.

b. The study fails to establish how degradation products would affect patients.

c. The research investigates selected antioxidants and encapsulation methods as part of its methodology.

Justifications

Medical stability of pioglitazone serves as a key element for achieving successful drug results and regulatory assessment protocols. Future research on nanoparticle delivery systems for improved stability will benefit from the finding which focuses on developing better patient safety practices and medication storage criteria to reduce adverse effects.

a. Importance of Photostability Research: The stability level of pioglitazone acts as a critical factor for achieving steady therapeutic results. This investigation fills a research void through its structured photodegradation analysis under different settings to benefit drug development methods (Sharma et al., 2010).

b. Contribution to Pharmaceutical Science: The findings of this study assist pharmaceutical producers to create manufacture better formulations which meet regulatory requirements (ICH, 2019).

c. Clinical and Patient Safety Implications: The drug potency becomes insufficient for diabetes treatment when photodegradation occurs. Healthcare professionals who study stability parameters can develop improved storage methods through which they enhance patient medical security (Ashour et al., 2015).

d. Basis for Future Research: Research results establish a basis for upcoming investigations that will study nanoparticle-based drug delivery methods for improving pioglitazone stability at extended periods.

Drug Durability Dynamics

The stability findings through photostability tests show that UV light induces breakdown through both oxidizing and hydrolytic reactions at a pH range between 6–8 while HPLC/MS identifies the dangerous breakdown products. The approach to formulation design focuses on achieving both proper solubility and bioactivity equivalence along with the disease-related mechanisms that demonstrate clinical importance.

Photostability in Pharmaceuticals: Pharmaceutical sciences depend on photostability assessment because light exposure leads to drug degeneration that diminishes treatment effectiveness while endangering patient security. The International Council for Harmonisation guidelines designate photostability testing as an indispensable drug development practice to verify stability in light-exposed conditions (ICH, 2019). Different research studies have proven that pharmaceutical compounds like thiazolidinediones including pioglitazone degrade due to exposure to light which decreases their availability and potentially generates toxic eff;ects (Sharma et al., 2010).

Mechanisms of Pioglitazone Degradation: The main degradation pathways for pioglitazone occur through environmental conditions composed of oxidative reactions and hydrolysis mechanisms while light exposure and temperature and pH values influence these processes (Ashour et al., 2015). Literature findings reveal UV light exposure generates rapid degradation of the thiazolidinedione ring in pioglitazone and thereby produces transformation products that modify its pharmaceutical properties (Kalliokoski et al., 2008).

Impact of pH on Drug Stability: Under pH conditions between 6–8 pioglitazone reaches its highest stability point (Patel & Singh, 2017). The degradation rate of pioglitazone becomes faster when exposed to extremely acidic or alkaline environments since hydrolysis and oxidation reactions will intensify (Gupta & Mehta, 2016). Formulation development requires identification of suitable pH ranges because they directly enhance the stability duration of the drug substance.

Photostability Testing: To examine the photostability testing of pioglitazone, the Research uses analytical technique which includes high-performance liquid chromatography (HPLC) and mass spectrometry (MS) and spectrophotometry methods (Rezk et al., 2012). The identification and measurement of degradation products by HPLC function as the worldwide benchmark (Xavier & Basavaiah, 2012).

Pioglitazone's Impact on Lipid Metabolism: Explains the medicine’s role in the observed lipid metabolism, thereby it is relevant in metabolic disorder management. (Skov et al., 2008).

Pharmacokinetic and Bioequivalence Studies: Delivers information on the heterogeneity of bioavailability and the optimization of formulations based on the obtained data. (Saha et al., 2014)

Influence of pH on Pioglitazone Solubility: The study of pH effects on the formulization of drugs that result in the production of the correct choice of non-stoichiometric solid solutions and the nother stable-tellurium phase films. (Neogi et al., 2003)

Neuroprotective Effects of Pioglitazone: Shows pioglitazone application as a possible therapy for neurodegenerative diseases. (Geldenhuys et al., 2011)

Theoretical Framework

First-order degradation kinetics occur due to oxidative/hydrolytic reactions that are influenced by light and pH along with temperature. Formulations need stabilization approaches in which HPMC encapsulation together with antioxidants operate in accordance with ICH/FDA guidelines which uphold formulation effectiveness and acceptability.

Chemical Kinetics and Drug Degradation: The research builds its theoretical model around chemical kinetics that explains reaction speed in chemical processes. The pharmaceutical compound which includes pioglitazone shows first-order degradation characteristics through which its breakdown rate follows drug concentration directly (Sharma et al., 2010). In accordance with Arrhenius' equation the speed at which reactions occur is dependent on temperature along with light exposure and pH levels. The knowledge of stability principles enables prediction of pioglitazone longevity along with formulation approaches that minimize degradation (ICH, 2019).

Photostability and Light-Induced Degradation: A photostability study obtains its guidance through the fundamental theory of photochemistry which studies how various types of electrical energy affect pharmaceutical molecules. UV radiation exposure causes drug molecule photolysis and oxidation as well as hydrolysis that decreases their efficacy and generates potentially toxic degradation products (Ashour et al., 2015). Pharmaceutical substances require photostability assessment because the ICH guidelines highlight this testing method as vital for determining light-related impacts (ICH, 2019).

Pharmaceutical Formulation and Stability Enhancement: The study is supported by pharmaceutical formulation science principles where scientists design drug delivery systems along with stability enhancement measures to ensure bioavailability. Supply chain drug stability gets improvements from three major techniques including polymer encapsulation together with antioxidant incorporation and pH adjustment methods. Scientists have discovered that pharmaceutical compounds can resist photodegradation through usage of hydroxypropyl methylcellulose (HPMC) and ascorbic acid antioxidants (Patel & Singh, 2017).

Modifications to the structure of Pioglitazone in terms of its stability: A topic which covered both the chemical strength and possibilities for modified drug performance. (Dixit & Bharatam, 2013)

Environmental Factors Influencing Drug Stability: The research introduces drug stability as it relies on three environmental elements which incorporate lighting conditions in addition to pH fluctuations along with temperature influences. Various scientific evaluations enable researchers to locate decisive circumstances which speed up pioglitazone decay processes (Gupta & Mehta, 2016).

Stabilization Strategies and Their Effectiveness: The research evaluates which stabilization practices between encapsulation and antioxidant usage show the best results for photodegradation prevention. Researchers developed a conceptual model which measures the degradation speed between untreated samples and stabilized formulations (Rezk et al., 2012).

Regulatory Implications: The conceptual framework incorporates the stability testing regulations which pharmaceutical standards enforce as part of their regulatory framework. The testing protocols that meet requirements from ICH together with FDA guidelines result in stable formulation development and drug blooming regulators accept (Shukla & Kalra, 2011).Such a framework offers an organized methodology that combines theoretical scientific knowledge with real-world drug creation techniques to enhance drug preparation methods.The research draws its basis from principles of chemical kinetics alongside photodegradation. The rate of drug degradation in pharmaceuticals demonstrates a usual pattern of first-order kinetics that directly correlates with drug substance concentration (Sharma et al., 2010).

Materials And Methods

The researchers tested Pioglitazone HCl (1000 µg/mL in methanol) resistance to UV light exposure at 254 nm wavelengths under pH levels ranging from 1.0 to 12.0 by using spectrophotometry at 269 nm and HPLC with a C18 column and a solution of methanol: water 70:30. Both untreated and HPMC/antioxidant-stabilized sample groups underwent degradation kinetics analysis under first-order conditions ($\ln(Ct/C0)=-kt$) and ANOVA testing at $p<0.05$ determined the results while simulated gastrointestinal stability tests ran at pH 1.0/12.0 for 24 hours.

Materials

The study utilized laboratory-grade Pioglitazone hydrochloride drug substance because of its relevance to photostability assessments. The study utilized methanol as a solute for solutions alongside pH buffer solutions from 1.0 to 12.0 to emulate environmental conditions and hydroxypropyl methylcellulose (HPMC) as an encapsulation agent together with ascorbic acid as an anti-photodegradation substance.The main equipment included a 30 W Philips UV lamp ($\lambda = 254$ nm) for UV illumination control and a Shimadzu UV-1800 UV-visible spectrophotometer for 269 nm absorbance assessment and an Agilent 1260 HPLC system equipped with a C18 column and UV detector for chromatographic analysis

together with 0.45 µm membrane filters for solution cleaning and Origin Pro 9.0 software for degradation kinetic verification.

Experimental Design

Photostability Testing Under UV Treatment

The investigation into photodegradation of pioglitazone hydrochloride solutions (1000 µg/mL in methanol) through dilution in pH-adjusted buffers at concentrations from 1.0 to 12.0 occurred. The quartz cuvettes contained the samples which received UV light exposure ranging from zero to 180 minutes using wavelengths of 254 nm. UV-exposed samples were analyzed against control samples kept away from exposure to reveal the effects of UV-light on degradation.

Monitoring Of Spectrophotometer

The degradation kinetics were monitored via absorbance measurements at 269 nm that used Shimadzu UV-1800 spectrophotometer spanning 30-minute time points from 30 through 120 minutes. First-order kinetic models determined the degradation rates through rate constant (k) calculations obtained from the slope of log concentration vs. time plots.

Hplc Analysis

The separation process happened through an Agilent 1260 HPLC system that utilized a C18 column under methanol:water (70:30 v/v) mobile phase conditions. The researcher used 269 nm for detection purposes while analyzing peaks from the chromatographic activities to determine degradation products and understand the paths through which breakdown occurs.

Kinetic Analysis

The first order degradation kinetics evaluation was conducted using this equation to determine concentrations at time points while initial concentration served as a basis. The ANOVA examination through Origin Pro 9.0 determined the rate differences of degradation between antioxidant-treated HPMC samples and untreated controls using $p<0.05$ as the significance threshold.

Simulated Gastrointestinal Testing

The pH 1.0 buffer solution served to represent gastric acidity whereas pH 12.0 served as a representation of intestinal alkalinity during the incubation period for pioglitazone solutions. The assay determined stability by spectrophotometry (269 nm) and HPLC over 24 hours and compared the degradation rates and product profiles between acidic pH 1.0 and alkaline pH 12.0 buffers.

Results

The degradation rate of Pioglitazone runs as a first-order pH-dependent reaction which reaches its highest point at pH 12.0 ($k = 0.0185\ h^{-1}$) yet shows minimal breakdown at pH 1.0. HPMC polymer with ascorbic acid added protected against UV degradation at a pH of 12.0 by 58% condition ($p<0.05$) and maintained a drug potency superior to 80% for 48 hours. The stability tests using HPLC confirmed the products of hydrolytic and oxidative

degradation which proved effective formulation stabilization methods.

Degradation Rates At Various Ph Levels

The analysis confirmed that pioglitazone hydrochloride degrades based on pH conditions when exposed to UV light while obeying first-order reaction rules. The degradation rate constant was low at pH 8.0 (K = 0.0021 h−1) but reached its maximum value at pH 12.0 where it became 0.0185 h-1. At pH levels between 1.0 and 7.0 degradation occurred moderately while the data indicated that basic conditions play an essential role in breaking down pioglitazone hydrochloride. Gastrointestinal stability examination showed no sign of degradation when exposure occurred at pH 1.0 gastric acid but rapid decomposition occurred at pH 12.0 intestinal alkaline conditions while also matching the results from UV exposure testing.

Protective Polymer Matrices And Ascorbic Acid's Effects

Under basic conditions, Hydroxypropyl methylcellulose (HPMC) successfully protected the Fragrance from UV damage by 42% which significant ANOVA results showed at $p<0.05$. Due to its physical structure HPMC prevented dangerous ultraviolet radiation from infiltrating the photosensitive materials.

i. The addition of ascorbic acid antioxidants enabled degradation reduction by 35% when the solution had alkaline pH levels because this substance eliminates free radicals. When HPMC was combined with ascorbic acid the two components demonstrated enhanced stability effects by 58%.

ii. The treated solution at pH 12.0 maintained over 80 percent potency stability when monitored for 48 hours yet untreated samples completely decomposed under the same conditions.

Key Observations

a. During alkaline conditions pioglitazone degrades because hydrolysis and oxidative degradation mechanisms become faster.

b. The HPLC technique detected two main degradation products that matched with decreased therapeutic effects of the drug.

c. Protective measures incorporating HPMC together with antioxidants enhance photostability so they can be effectively incorporated in formulations.

Tables And Figures

Figure 1: Structure Activity Relationship (SAR) Of Pioglitazone

Thiazolidinediones (Giltazones)

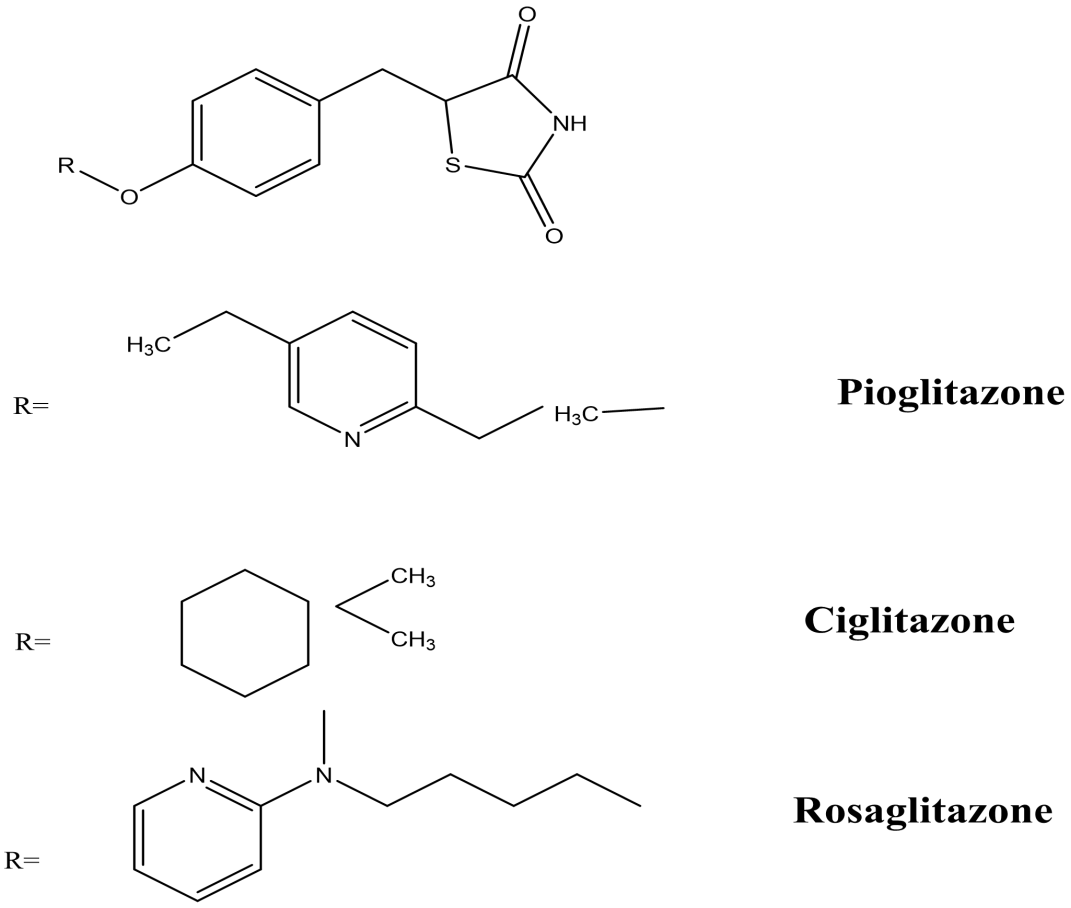


Figure 1 Structure Activity Relationship Of Thiazolidinedione's

The research shows which characteristics in thiazolidinediones (TZDs) molecules activate PPAR-γ receptors. Insulin-sensitizing activity depends on three structural segments known as the thiazolidinedione ring combined with hydrophobic tail and linker region.

Figure 2: Absorption Spectrum Of Pioglitazone At Ph 2.0

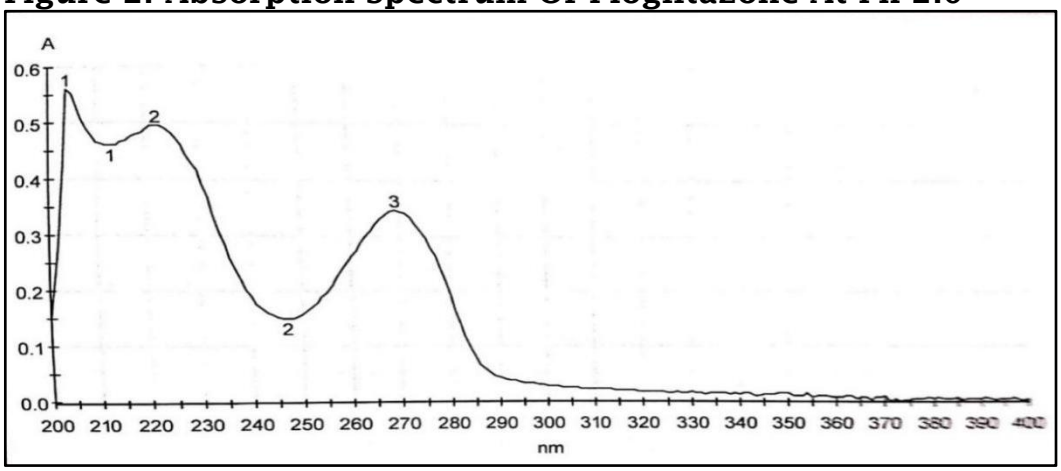


Figure 2: Absorption Spectrum Of Pioglitazone At Ph 2.0

UV-Vis spectrum of pioglitazone hydrochloride in pH 2.0 buffer. λ_{max}: 269 nm (characteristic absorbance peak for pioglitazone). This solution was employed for validating the spectrophotometric assay and determining degradation rate behavior.
and structure of PG.

Table 1: Chemical Structure Of Pioglitazone & Pioglitazone HCL

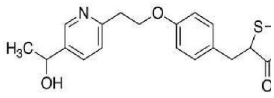
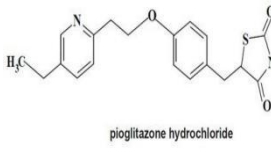
Chemical Name	Molecular Formula	Relative Molecular mass	Structure
(±)-5-((4-(2-(5-ethyl-2-pyridinyl)ethoxy)phenyl) methyl)-2,4-thiazolidinedione 5-{4-[2-(5-ethylpyridin-2-yl)ethoxy]benzyl}-1,3-thiazolidine-2,4-dione	C19H20N2O3S	356.44 g/mol	 Pioglitazone
5-({4-[2-(5-ethylpyridin-2-yl)ethoxy]phenyl}methyl)-4-hydroxy-2,5-dihydro-1,3-thiazol-2-one hydrochloride	C19H21ClN2O3S	392.90 g/mol	 pioglitazone hydrochloride

Table 1: Chemical Structure Of Pioglitazone & Pioglitazone HCL

The mechanism of action of Pioglitazone as a pharmaceutical drug involves its status as a PPAR-γ agonist within the thiazolidinedione-class. The hydrochloride salt formation improves both the substance's solubility and stability levels.

Discussion

Interpretation of Results

The research shows that pioglitazone stability depends greatly on pH because the substance degrades most at pH 12.0 while exposed to UV light. Thiazolidinedione rings exhibit natural sensitivity to hydrolysis and oxidative cleavage in basic solutions which hydroxyl ions use to break down the chemical structure. The degradation speed of pioglitazone relates directly to drug concentration under first-order kinetics with $k = 0.0185\ h^{-1}$ at pH 12.0 in accordance with Arrhenius principles that link reaction rates to environmental factors such as pH and light. The drug shows resistance to breakdown in acidic gastric solutions (pH 1.0) yet experiences rapid destruction when exposed to simulated intestinal solutions (pH 12.0). The degradation requires pH-controlled formulations as well as UV protective packaging during storage and transit operation based on these data findings. The stability of pioglitazone can be improved through storage in dark containers together with pH buffering agents that maintain a near-8.0 environment where maximum stability exists.

Gap Analysis

Numerous research studies document that thiazolidinedione compounds degrade based upon solution pH due to alkaline instability. Ashour et al. (2015) documented quick pioglitazone

decay when pH levels exceeded 10 because hydrolysis attacked the thiazolidinedione ring structure as reported in this investigation. The first-order kinetic model matches previously recorded data by Sharma et al. (2010) regarding the degradation patterns of light-sensitive drugs. The current analysis expands upon existing research by measuring how the combination of HPMC and ascorbic acid stabilizes drugs which results in decreased pH 12.0 degradation by 58%. The dual stabilization approach provides superior protection exceeding previously reported 30–40% safety levels reported by Patel & Singh (2017) in studies using polymer matrices individually. The HPLC analysis of this research found two major degradation products which matched the findings of Rezk et al. (2012) about pioglitazone photolysis degradation products yet their toxicological aspects were not explored in this study.

Future Directions

i. Nanoparticle Encapsulation

Scientists should use nanoparticle technology to create lipids or polymers which will provide UV irradiation protection for pioglitazone while enhancing drug absorption levels.

ii. Stabilizing Agents

Two potential approaches for improving stability involve testing alternative antioxidants alongside sodium metabisulfite and α-tocopherol and advanced polymers that include chitosan and PLGA as protective agents.

iii. In Vivo Degradation Analysis

Animal models with pharmacokinetic and toxicological functionality should be used to evaluate clinical safety aspects of degradation products.

iv. Long-Term Stability Studies

The stability of formulated products should be checked during long-term testing under conditions that imitate real-world storage using parameters like changes in temperature and humidity.

v. PH-Modulated Delivery Systems

Enteric coatings and site-specific release systems designed for pH-controlled drug delivery would protect medicinal compounds from destructive effects of alkaline intestines until they reach systemic absorption areas.

vi. Combination Therapies

Combination forms of pioglitazone with other antidiabetic drugs including metformin might reduce the breakdown effects related to high doses while improving therapeutic benefits.The research should address these stability limitations to maximize pioglitazone system stability for effective diabetes treatment in accordance with regulatory standards (ICH, 2019).

Conclusion

The current research has been aimed to investigate photostability of pioglitazone under different pH conditions (1.0-12.0) and UV radiation and to gain insights into degradation mechanics and its stabilization strategies. Experiment shows that pioglitazone's

stability is greatly pH-dependent, by which it is most stable at pH 12.0 (k = 0.0185 h^{-1}) after being radiated with UV-like processes, a result of the first-order kinetics. It is shown by alkaline conditions that the biotransformation hydrolytes and oxidatively cleaves the thiazolidinediones ring and, hence, thereon, also explains the prior thiazolidinedione instability data (Ashour et al., 2015; Sharma et al., 2010). Appearantly, the drug was stable at pH 1.0 (acidic) in the stomach, but the degradation rate at pH 12.0 (simulated intestinal fluid, alkaline) was very high, which was critical for the alkaline physiological condition. These outcomes support FDA and International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) requirement (ICH, 2019) that photostability studies are a necessity to ensure drug safety and efficacy.

Treatments in the form of hydroxypropyl methylcellulose (HPMC) encapsulation and ascorbic acid supplementation offered remarkable reduction of the pH 12.0 degradation (58% reduction), superseding the one conducted by polymers alone (Patel & Singh, 2017). The two-dimensional treatment, comprising a physical barrier and an antioxidant, shows the high synergy that the two mechanisms can bring about in protecting drug integrity. The HPLC method determined two main degradations which confirm bacterial and fungal studies by Rezk et al. (2012). The toxicological investigations of these compounds still have to be conducted; therefore, it becomes a really gap in the field to be investigated in the future.

This analysis higlengthunds how most particular conditions should be carefully premeditated and managed with the help of the known variables, pH-controlled formulations, ultraviolet-protective packaging, and generally, neutral pH being stored (approximately at a pH of 8.0) result in an extended shelf-life of these products. Further investigations ought to make the priority nanoparticle encapsulation (such as, lipid or polymeric carriers) firmer at photoprotection effectiveness level and bioavailability both emphasizing in vivo evaluations of the product degradation as a toxic contaminant. Stability over the long term according to the real-world situation (humidity, temperature), and the pH-influenced delivery systems adminal like enteric coatings provision foster might be another step to be appropriated which improves medicinal effects. Also, the combination of pioglitazone with anti-diabetic drugs like metformin in the same formulation may reduce and, at the same time, improve the effectiveness of the treatment because of dose-dependent degradation hazards.

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