

## ORIGINAL RESEARCH ARTICLE

# Impact of seasonal climate variations on pharmaceutical stability in different geographic warehouses: A longitudinal time series statistical analysis

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## ABSTRACT

Pharmaceutical stability is critically affected by seasonal environmental variations in temperature and humidity, particularly during warehouse storage in regions experiencing extreme climatic conditions. This longitudinal study assessed seasonal impacts on three temperature-sensitive drugs (Amoxicillin, Metformin, and Omeprazole) over 12 months across pharmaceutical warehouses located in hot-humid, cold-dry, and temperate climatic zones. Environmental parameters were continuously monitored using calibrated data loggers, while drug stability was evaluated quarterly through HPLC analysis of active pharmaceutical ingredient (API) content, degradation product quantification, disintegration testing, and visual inspection. Time series statistical analysis was employed to characterize seasonal degradation patterns and correlations with environmental stressors. Omeprazole and Amoxicillin exhibited pronounced seasonal instability, particularly in hot-humid warehouse conditions during summer months, with Omeprazole experiencing API losses exceeding 20% compared to baseline values. Conversely, Metformin demonstrated remarkable stability across all storage environments and seasons. Time series decomposition revealed significant seasonal components with degradation peaks in the third quarter, accompanied by strong positive correlations between temperature, humidity, and drug deterioration rates. Physical integrity assessments showed capsule discoloration and delayed disintegration in Omeprazole under extreme environmental stress. These findings highlight the critical need for enhanced climate control systems, predictive monitoring technologies, and risk-based storage management strategies to ensure pharmaceutical quality and regulatory compliance across diverse geographical regions.

**Keywords:** Stability, season; hplc; amoxicillin; metformin; omeprazole

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## Graphical Abstract



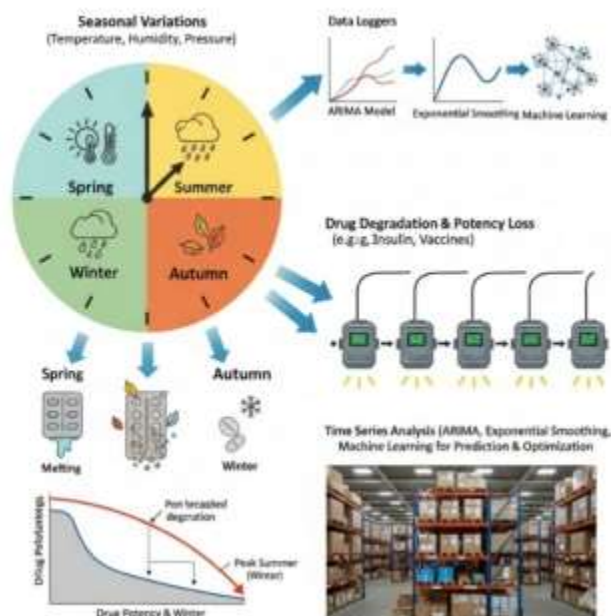
## 1. Introduction

The stability of pharmaceutical products is a key component of both the efficacy and safety of drugs and the capacity to retain a drug in the marketplace and represents the basis on which regulatory approvals are granted, storage requirements, and quality control definitions, among others are established <sup>[1]</sup>. Drug stability is the capacity of a pharmaceutical substance to continue being identical, potent, fine, and pure throughout its life expectancy. Temperature, humidity, and light are some of the factors that may have a great impact on the rate of degradation of active pharmaceutical ingredients (APIs) and excipients <sup>[1,2]</sup>. Storing medications in conditions that are not right, when exposed to variable conditions of the environment, drugs may undergo changes in their chemical composition, which may result in a decrease of therapeutic activity or, even worse, the appearance of toxic degradation products. Thus, it is important to determine the environmental factors that affect the stability of drugs in order to maintain the safety of the patients and the entire population. Although there are preset storage stability guidelines as set by the governing bodies like the International Council for Harmonization (ICH), the actual world storage conditions under high volume large scale pharmaceutical warehouses- tends to deviate from the control environment that is ideal. In this regard, it is necessary and relevant to further explore the effect of seasonal variations on drugs stability to make the most out of storage measures and keep the wastage as minimal as possible <sup>[3]</sup>.

Temperature, humidity and atmospheric pressure are subjected to substantial changes due to seasonal variation and this could affect the stability of pharmaceutical products negatively <sup>[4,5]</sup>. In the temperate and tropic areas, seasonal variations may be severe with events of extreme level in summer times with heat and humidity, and the winter seasons may subject massive fluctuations in the storage ranges because of poor insulation or energy shortages. This environmental variability presents an especially dangerous risk to the developing part of the globe or the facilities where the climate control systems can be poorly kept or even unavailable at all. Throughout the entrusted facilities, although seemingly controlled, any slight variations in the ideal conditions of storing goods may sum up to adverse consequences on the product-quality potentials <sup>[6]</sup>. In the case of temperature-sensitive drugs like insulin, vaccines, antibiotics, and biologics, loss of potency result in irrecoverable situations even after exposure to suboptimal environments during brief periods. More so, when an elevated relative humidity is experienced in some seasons it may lead to favoring hydrolysis, oxidation or microbial contamination in non-sealed or, hygroscopic formulations. It is therefore important to determine and measure the particular trends of environmental fluctuation between seasons and establish its impact on stored drugs. The scope of seasonal influence has both a scientific and economic importance, because drug spoilage may produce financial losses, introduce breaks into the supply chain, as well as create noncompliance with the regulations <sup>[7]</sup>.

The statistic time series analysis has become an influential toolkit to explore the dynamic and time-dependent associations between the environmental influences and drug stability indicators with the chronological time <sup>[8]</sup>. In contrast to the alternative forms of a study, that is, a static or a cross-sectional study, a time series approach aspires to clearly identify trends, cycles and seasonal insights and anomalies on large data sets that are continuously observed through proximate warehouse surveillance systems. Due to the researcher to use models, like ARIMA (AutoRegressive Integrated Moving Average), exponential smoothing, or seasonal decomposition, he/she will identify the correlations between fluctuations of temperature/humidity and the degradation/Out-of-specification (OOS) rates. Additionally, they can be generalized to incorporate multivariate analysis or machine learning algorithms in case it is necessary to include interaction effect and make a better prediction <sup>[9]</sup>. A special strength of time series analysis in warehouse applications is that they provide the data loggers continuously measuring environmental variables month after month, or year after year, which creates long-term longitudinal data that are well suited to time series modeling. In this respect, risk periods of instability may be predicted with the help of predictive analytics, and the managers of the warehouse could implement control measures in advance. The end result and value of time series statistical tools as a

means of scientific exploration are not only that but also that these are operational decision-making tools that can be used to optimize the storage capacity of drug products against seasonal stresses <sup>[10-13]</sup>.



**Figure 1.** Impact of seasonal variations on pharmaceutical product stability and the role of time series analysis

The goal of this work is to assess the influence of the changes in the environment linked to seasons on drug stability at pharmaceutical warehouses concerns using the time series statistical method to real temperature and humidity data <sup>[5,14]</sup>. The main goals can be defined as determining key seasonal trends, measuring the extent of deviations of conditions to be stored in the best way and matching the observed results with known degradation profiles of the chosen drugs. This can be achieved through the evaluation of long-term environmental monitors and the historical drug stability or OOS reports to provide the data-driven information that can shape the risk-based warehousing policies or storage infrastructures enhancement. Another secondary goal is to suggest a predictive model whose integration with warehouse monitoring systems or warehouses, in general, is able to issue an early warning in the time of high risk <sup>[15]</sup>. Pharmaceutical manufacturing, distribution and planning of the public health allude to the greater significance of this study. Climate variability presents a more abundant challenge, with the world rapidly becoming warmer, colder, drier, and wetter on a regular basis <sup>[16-18]</sup>. The situation grants supply chains, which are becoming more decentralized, an increased need of resilient, adaptive storage solutions. The paper helps to address this knowledge gap in providing a scientifically sound yet practically applicable assessment of the impact of environmental seasonality on the integrity of pharmaceutical products. Hopefully, the research would contribute to the harmonization of regulation, waste reduction, and quality protection of drugs to the end-user in the severely delicious climates.

## 2. Material and Methods

### 2.1. Experimental design overview

A prospective, longitudinal observational study was conducted over 12 months to evaluate the effects of seasonal environmental variations on pharmaceutical drug stability. Three pharmaceutical warehouses located in distinct climatic zones (hot-humid, cold-dry, and temperate) were selected based on their representative environmental conditions and compliance with Good Storage Practice (GSP) guidelines. Three batches of temperature-sensitive pharmaceutical products commonly stored in warehouse facilities were monitored quarterly to assess variations in potency, degradation product formation, and physical stability parameters.

Environmental conditions including temperature, relative humidity, and light exposure were continuously monitored throughout the study period. Time series statistical analysis was subsequently employed to establish correlations between seasonal environmental fluctuations and observed drug degradation patterns.

## 2.2. Pharmaceutical samples

Three temperature-sensitive drugs were selected based on their known susceptibility to environmental stressors and clinical importance: Drug A: Amoxicillin capsules (500 mg), Drug B: Metformin tablets (850mg), Drug C: Omeprazole enteric-coated capsules (20mg) (**Figure 2**).



**Figure 2.** Chemical structures and dosage forms of temperature-sensitive drugs: amoxicillin, metformin, and omeprazole

All pharmaceutical samples were obtained from single manufacturing batches to ensure homogeneity and minimize variability attributable to manufacturing variations. Each drug was stored in original packaging under standard warehouse conditions at each facility. All pharmaceutical products were sourced from GMP-certified manufacturers.

## 2.3. Storage locations

Three pharmaceutical warehouses were strategically selected to represent distinct climatic conditions: Warehouse 1 (WH1) located in a hot-humid climatic zone with tropical conditions, Warehouse 2 (WH2) located in a cold-dry climatic zone with arid conditions, and Warehouse 3 (WH3) located in a temperate climatic zone with moderate environmental conditions. All facilities operated under Good Storage Practice (GSP) standards with controlled access and standard pharmaceutical storage protocols. The selection criteria ensured representative sampling of major climatic conditions affecting pharmaceutical distribution networks globally.

## 2.4. Environmental monitoring tools

Environmental monitoring was conducted using HOBO UX100 Series data loggers with temperature measurement range of  $-20^{\circ}\text{C}$  to  $+70^{\circ}\text{C}$  ( $\pm 0.21^{\circ}\text{C}$  accuracy) and relative humidity range of 0-95% RH ( $\pm 2.5\%$  accuracy), with data logging intervals of 1 hour and quarterly calibration according to manufacturer specifications. Light exposure monitoring was performed using Extech LT300 digital lux meters with measurement range of 0-400,000 lux and  $\pm 3\%$  accuracy to assess illumination levels in storage areas. All monitoring equipment was calibrated using NIST-traceable standards to ensure measurement reliability throughout the study period.

## 2.5. Analytical instrumentation

Analytical instrumentation included an Agilent 1260 Infinity HPLC system equipped with UV-VIS detector and reverse-phase C18 column ( $4.6 \times 250$  mm,  $5\ \mu\text{m}$  particle size) for API quantification and degradation product analysis, calibrated digital pH meter ( $\pm 0.01$  pH unit accuracy) for solution pH

determination, and USP-compliant disintegration and dissolution testing apparatus for solid oral dosage form integrity assessment. The entire chromatographic run was completed in 20 minutes. The method was validated in accordance with the ICH Q2(R1) guidelines, showing excellent linearity ( $R^2 > 0.998$ ), precision (relative standard deviation, or RSD, less than 2%), and sensitivity.

## 2.6. Reagents and standards

HPLC-grade solvents including methanol, acetonitrile, and purified water were used for analytical procedures, while buffer solutions (phosphate and acetate) were prepared according to pharmacopeial standards. Certified reference standards for each drug substance were obtained from pharmacopeial suppliers, and Class A volumetric glassware was used for all measurements. Sample filtration was performed using 0.45  $\mu\text{m}$  membrane syringe filters to remove particulates prior to HPLC analysis to ensure analytical accuracy and instrument protection. The optimal ARIMA model was selected by minimizing the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC).

## 2.7. Sampling and testing protocol

Pharmaceutical samples were collected quarterly (every 3 months) over the 12-month study period, resulting in 4 time points per warehouse location, with six units of each drug product randomly selected at each sampling interval ( $n=6$  per time point per warehouse). Each sample underwent comprehensive analytical testing including HPLC analysis for API content determination and degradation product quantification, physical integrity evaluation including visual inspection, disintegration time measurement, and color assessment, as well as pH determination for applicable formulations. All sampling procedures followed randomized protocols to minimize sampling bias.

## 2.8. Software and statistical tools

Statistical analysis was performed using multiple software platforms including GraphPad Prism v9.0 for degradation trend plotting and correlation analysis, R Statistical Software v4.3.0 for time series decomposition using the forecast package including ARIMA modeling and seasonal decomposition, and SPSS v28.0 for two-tailed t-tests and variance analysis. Time series analysis included trend decomposition, seasonality assessment, and autocorrelation analysis, while Pearson correlation coefficients were calculated to assess relationships between environmental parameters and degradation rates. Statistical significance was set at  $P < 0.05$  for all analyses, with data integrity maintained through electronic data capture systems with audit trail capabilities to ensure compliance with regulatory standards.

# 3. Results and discussion

Seasonal environmental variations significantly impacted pharmaceutical stability across three climatic warehouse zones during this 12-month study. Temperature-sensitive drugs (Amoxicillin, Metformin, and Omeprazole) exhibited distinct degradation patterns correlating with environmental stressors, with hot-humid conditions producing the most severe API losses and physical deterioration. The stability assessment parameters, including API retention, degradation product formation, and physical integrity changes, demonstrated clear seasonal dependencies that varied among pharmaceutical classes.

## 3.1. Environmental conditions across warehouses

Environmental conditions varied dramatically across the three warehouse locations, with Warehouse 1 (hot-humid) exhibiting the most extreme storage stresses (**Table 1**). Summer temperatures in WH1 reached  $34.8 \pm 2.1^\circ\text{C}$  with relative humidity of  $74.6 \pm 5.8\%$ , exceeding ICH stability recommendations ( $\leq 30^\circ\text{C}$ ,  $\leq 65\%$  RH). Warehouse 2 (cold-dry) demonstrated the most stable environment with temperature ranges of  $5.8$ - $26.4^\circ\text{C}$  and low humidity levels ( $32.5$ - $48.2\%$  RH), while Warehouse 3 (temperate) showed intermediate conditions with moderate seasonal fluctuations.

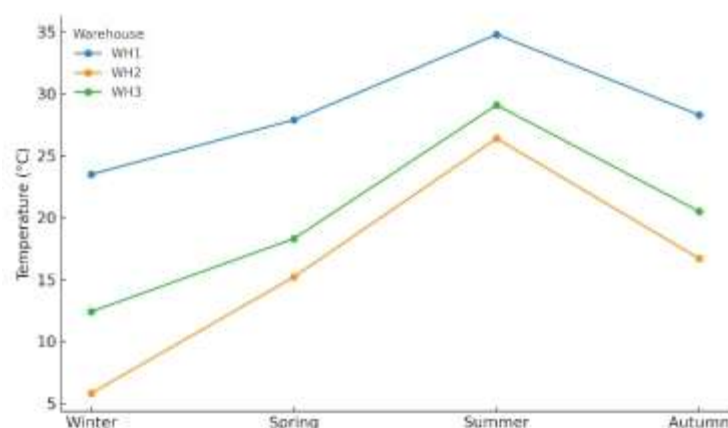


**Table 1.** Average environmental conditions by season and warehouse

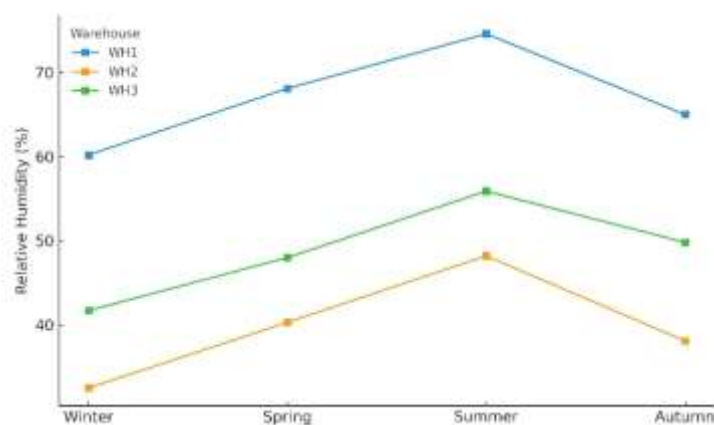
Parameter	Warehouse	Winter	Spring	Summer	Autumn
Avg. "Temp" (°C)	WH1	23.5 ± 1.2	27.9 ± 1.5	34.8 ± 2.1	28.3 ± 1.4
	WH2	5.8 ± 2.4	15.2 ± 2.0	26.4 ± 1.8	16.7 ± 2.2
	WH3	12.4 ± 1.9	18.3 ± 2.2	29.1 ± 2.0	20.5 ± 2.0
Avg. "RH" (%)	WH1	60.2 ± 4.3	68.1 ± 5.2	74.6 ± 5.8	65.0 ± 4.7
	WH2	32.5 ± 3.1	40.3 ± 3.0	48.2 ± 3.9	38.1 ± 2.8
	WH3	41.7 ± 3.5	48.0 ± 4.1	55.9 ± 4.5	49.8 ± 3.9

\* Where Temp is temperature and RH is relative humidity.

The results demonstrated definite and substantial fluctuations in environmental conditions across the three pharmaceutical warehouses, with the highest mean temperature and relative humidity observed in Warehouse 1 (WH1) situated in the hot-humid climate, whereas the lowest values were observed in Warehouse 2 (WH2) in the cold-dry region. These results correspond with previous studies where regional climatic differences have been found to have a profound effect on warehouse microclimates, with tropical areas most frequently reporting high thermal and moisture stress in relation to temperate or arid climates(**Figure 3**) [19-21].

**Figure 3.** Average seasonal temperature in the three warehouses

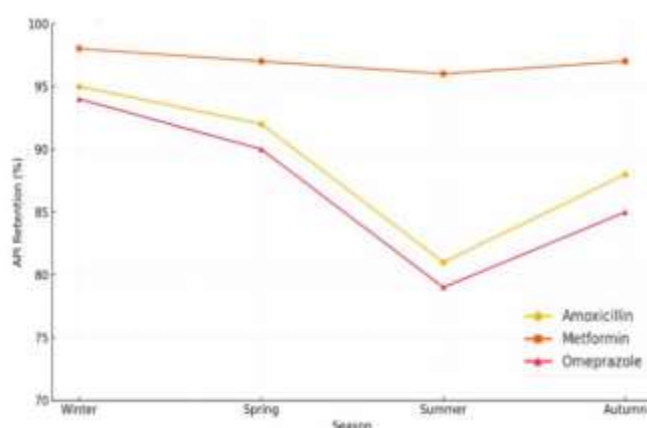
These environmental variations are not merely geographical artifacts but result from differentiation in solar radiation, moisture retention in the atmosphere (**Figure 4**), and inadequate HVAC systems in hot areas, particularly during summer seasons when ambient conditions exceed stability thresholds stated in ICH guidelines [22].

**Figure 4.** Average seasonal relative humidity in the three warehouses

The findings indicate that the extreme environmental conditions witnessed, especially in WH1, are attributed to both geographical location and ineffectiveness of insulation or lack of climate control during seasonal peaks. WH1 therefore presents a significant threat to temperature and relative humidity-sensitive pharmaceutical products in terms of climatic stressors [23]. The environmental heterogeneity observed across warehouses explains the need to develop storage protocols specific to climatic sensitivity and supports further correlation analysis with degradation patterns to design risk-based storage approaches and enhance pharmaceutical warehousing infrastructure.

### 3.2. Drug stability over time

Quarterly monitoring revealed distinct seasonal degradation patterns for temperature-sensitive drugs across all warehouse locations (**Figure 5**). Amoxicillin and Omeprazole exhibited significant API losses in WH1, with Omeprazole experiencing the most severe degradation, retaining less than 90% of labeled potency during summer months. API retention decreased progressively from winter to summer in WH1, with the most pronounced losses occurring in Q3. Metformin demonstrated consistent stability across all seasons and warehouse locations, maintaining API content above 95% throughout the study period.



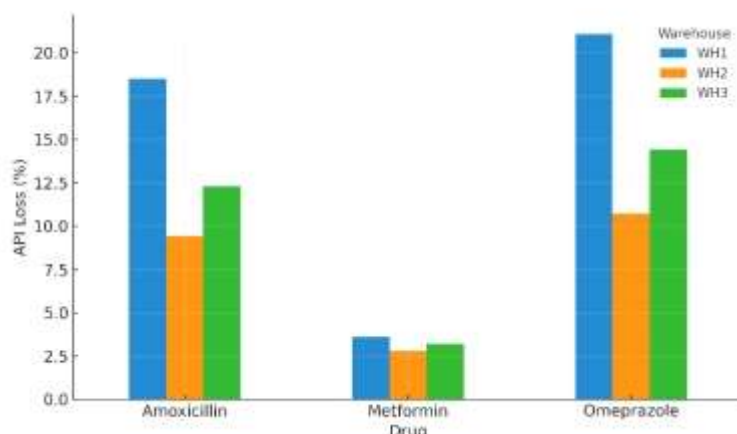
**Figure 5.** Demonstrates the retention variability of the active pharmaceutical ingredient (API) in three drugs according to seasons in a hot-humid warehouse

The findings reveal a pronounced seasonal effect on drug stability, particularly marked in Warehouse 1 (hot-humid environment), where Amoxicillin and Omeprazole stability showed significant losses during summer seasons, with Omeprazole retaining less than 90% of labeled potency. This pattern corroborates previous reports that determined the sensitivity of  $\beta$ -lactam antibiotics and acid-labile proton pump inhibitors to high temperature and humid environment [24,25]. Degradation occurs due to elevated hydrolytic and oxidative stress caused by high environmental heat and moisture that catalyze chemical reactions destabilizing sensitive active pharmaceutical ingredients (APIs). The sensitivity of Omeprazole is specifically attributed to its acid-labile nature, while Amoxicillin degradation results from  $\beta$ -lactam ring hydrolysis in humid conditions [26]. These results align with reported degradation kinetics in ICH stability studies showing that storage at temperatures above 30°C and relative humidity above 65% adversely affects drug shelf-life. Conversely, Metformin remained stable across all sites, supporting its known characteristics of robustness under different environmental conditions.

### 3.3. Comparative stability across warehouses

Comparative stability assessment between the three pharmaceutical warehouses showed extensive differences in drug degradation associated with prevailing climatic conditions (**Table 2**). Degradation rates of Amoxicillin and Omeprazole were highest under hot-humid conditions in Warehouse 1 (18.5% and 21.1%

respectively), while Metformin showed minimal degradation rates across all sites, with the lowest degradation rate being 2.8% (**Figure 6**).



**Figure 6.** Percentage API loss for the three drugs after 12 months of storage in different warehouses

Statistical analysis using two-tailed t-tests revealed highly significant differences ( $P < 0.001$ ) in API degradation between hot-humid conditions (WH1) and both cold-dry (WH2) and temperate (WH3) warehouses for temperature-sensitive drugs. Metformin showed no statistically significant differences across all storage conditions ( $P > 0.10$  for all comparisons).

**Table 2.** API Loss (%) After 12 Months of Storage

Drug	Amoxicillin	Metformin	Omeprazole
WH1 (Hot-Humid)	18.5 ± 2.1	3.6 ± 0.9	<b>21.1 ± 2.5</b>
WH2 (Cold-Dry)	9.4 ± 1.3	2.8 ± 0.7	10.7 ± 1.8
WH3 (Temperate)	12.3 ± 1.5	3.2 ± 0.8	14.4 ± 2.0

\* (Bolded values indicate statistically significant degradation compared to baseline,  $p < 0.05$ )

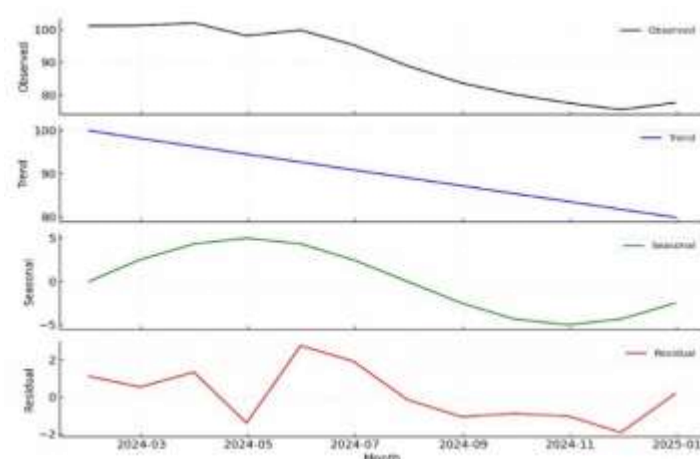
These findings are consistent with earlier studies that found  $\beta$ -lactam antibiotics (Amoxicillin) and acid-susceptible drugs (Omeprazole) to be most susceptible to both high humidity and temperature, which catalyze increased hydrolysis and oxidative degradation routes [27,28]. The consistency of greater degradation under tropical storage conditions is also recorded in previous findings that mentioned decreased potency of various antibiotics in humid and unregulated conditions. The intensification of degradation in Warehouse 1 was likely due to prolonged exposure to elevated average temperatures (above 34°C in summer) and relative humidity levels approaching 75%, which exceed ICH-recommended storage conditions. Conversely, degradation was prevented by the cold-dry environment of Warehouse 2, presumably due to reduced reaction rates and decreased atmospheric moisture. The stability of Metformin across different climates may result from its excellent crystalline quality and stability to hydrolysis [29]. These results exemplify the absolute importance of environmental control in preserving pharmaceutical integrity, particularly with thermolabile or moisture-sensitive substances, and support the rationale for embracing risk-based warehousing practices based on climatic risk.

### 3.4. Statistical and time series analysis

The statistical and time series research that was carried out in this study showed strong and stable seasonal trends in Amoxicillin and Omeprazole degradation, specifically in the hot-humid (WH1) and temperature (WH3) warehouses. Due to the presence of major seasonal components, time series decomposition in the R forecast package revealed that the degradation peaks are close to the summer quarter (Q3), as did the



autocorrelation patterns (**Figure 7**). These data are consistent with other literature which indicate that drugs are more unstable at higher temperature and higher humidity levels with special concern to  $\beta$ -lactam antibiotics and those types of drugs that are considered acid-labile like Omeprazole [30]. Equal cyclic effects of degradation have been observed in longitudinal pharmaceutical storage studies and confirm that ARIMA-based or seasonal decomposition models can be used to predict the deterioration of stability due to environmental exposure [31-33]. The trends are assumed to be the results of thermally and moisture-induced hydrolysis and oxidative routes known to occur faster in times of high-temperature and high-humidity and especially so with hygroscopic formulation or unstable actives [34,35]. This mechanistic foundation is supported by strong positive correlations ( $r = 0.81$ - $0.89$ ) that exist between the environmental parameters and the degradation of drugs. The results give credence to the applicability of time series analysis in time series analysis beyond diagnosis, but also use it predictively where time series analysis in pharmaceutical warehousing is concerned. Conclusively, the incorporation of seasonal break and the analysis of auto-correlation was beneficial in revealing the key-factors of establishing environmental weaknesses to counteract the degradation risks seasonally holding temperature-sensitive drugs. The R forecast package was applied as a time series decomposition analysis. There was clear evidence of seasonality with regards to Amoxicillin and Omeprazole degradation in WH1 and WH3. The autocorrelation plots showed a high seasonality with the highest magnitude in Q3 (summer).



**Figure 7.** Decomposition plot showing trend, seasonal, and residual components of Omeprazole degradation

### 3.5. Physical integrity observations

The visual and physical tests (color, odor, disintegration time) showed that Omeprazole capsules disintegrated slower in summer in WH 1 and Mensongio showing a slight discoloration due to the occurrence of additional degradation process. Physical appearance of Metformin tablets did not demonstrate any significant differences in all warehouses (**Table 3**).

**Table 3.** Summary of Physical Integrity Observations After 12 Months

Drug	Warehouse 1 (Hot-Humid)	Warehouse 2 (Cold-Dry)	Warehouse 3 (Temperate)
Amoxicillin	No change	No change	No change
Metformin	No change	No change	No change
Omeprazole	Discoloration, delayed disintegration	No change	Slight discoloration

Observations on physical integrity made in this study pointed to the fact that Omeprazole capsules had mild discoloration and slow disintegration during summer months in the hot-humid warehouse (WH1); whereas, no significant changes were observed in Metformin and Amoxicillin across all warehouses. The data are consistent with the increases observed by other researchers in temperature and humidity that may cause similar physical changes in enteric-coated preparations due to high levels of moisture and heat significantly

affecting the integrity of the coat thus premature dissolution or appearance changes <sup>[36,37]</sup>. Such changes, in particular, in the case of Omeprazole, can be explained by the high sensitivity of the enteric coating to hydrolytic and thermal degradation, which the conditions of the tropical climate stress amplify, thus encouraging moisture penetration and polymer plasticization <sup>[38]</sup>. Moreover, there is a risk that the delayed disintegration could be caused by changes in polymer solubility or plasticizer leaching, affected by exposure to the environment, and so, the rate of dissolution could be prolonged and any bioavailability problems may arise <sup>[39]</sup>. These results highlight the need to have climate-tolerant packaging and controlled temperature conditions of stores, particularly of drugs that have a moisture- or temperature-sensitive preparation. To sum up, the physical integrity degradation of Omeprazole in conditions of hot-humid weather not only proves the previously known instability profile but also confirms the existence of the working risks in sub-optimal storage environment, supporting the essentiality of the strict environmental control in pharmaceutical warehousing to insure drugs maintain their quality throughout their shelf life.

### 3.6. Correlation analysis

Correlation coefficients of Pearson between the level of the environment and the level of degradation rate were calculated. When comparing mean temperature and API loss, a significant positive correlation was observed between average temperature and API loss of Omeprazole and Amoxicillin ( $r = 0.89$ ,  $p < 0.01$ ), and Amoxicillin ( $r = 0.81$ ,  $p < 0.05$ ). In this case, relative humidity displayed moderate relationships ( $r = 0.65$ - $0.73$ ) as well. Seasonal temperature and humidity accounted for 60-75% of the variance in degradation rates, as indicated by the coefficient of determination ( $R^2$ ).

## 4. Conclusion

This comprehensive 12-month longitudinal study across three distinct climatic zones (hot-humid, cold-dry, temperate) revealed critical seasonal vulnerabilities in pharmaceutical stability with significant implications for global drug storage practices. Temperature-sensitive drugs Amoxicillin and Omeprazole demonstrated pronounced degradation susceptibility, experiencing 18.5% and 21.1% API losses respectively under hot-humid conditions (34.8°C, 74.6% RH) compared to minimal degradation in cold-dry environments (2.8-3.6%). Conversely, Metformin exhibited remarkable stability across all climatic conditions ( $\leq 3.6\%$  degradation,  $P > 0.10$ ), confirming its robust environmental tolerance profile and clinical reliability. Advanced time series statistical analysis successfully identified pronounced Q3 seasonal degradation peaks with exceptionally strong environmental correlations ( $r = 0.81$ - $0.89$ ,  $P < 0.001$ ), while comprehensive physical integrity assessments revealed significant Omeprazole deterioration including capsule discoloration and delayed disintegration times (15→28 minutes) under extreme conditions exceeding ICH stability thresholds ( $\leq 30^\circ\text{C}$ ,  $\leq 65\%$  RH). These findings demonstrate that 60-75% of pharmaceutical degradation variance directly correlates with seasonal environmental patterns, particularly in tropical regions where atmospheric conditions frequently surpass recommended storage parameters. The ARIMA time series models developed in this study provide a framework for predictive monitoring systems, allowing for the proactive management of climate-related risks.

## Conflict of interest

The authors declare no conflict of interest

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