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A One-Year Environmental and Microbiological Monitoring of Storage Areas and Production Room of a Pharmaceutical Industry from Northern Nigeria

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Abstract

The degradation and reduction of the potency of both raw materials and finished pharmaceutical products (FPPs) are of great concern to pharmaceutical industries, making the environmental monitoring of storage areas and production rooms a must. In this study, a one year monthly data for environmental and microbiological monitoring for storage areas (raw materials quarantine room, raw materials approved room, finished product quarantine room and finished product approved room) and production room were collected and analyzed using IBM SPSS Statistics Version 23. The results revealed that the lowest temperature (21.01°C) was obtained from the raw materials approved room. At the same time, the highest (29.50°C) was recorded from the finished product quarantine room. In contrast, the lowest relative humidity of 11.11% was obtained from raw materials quarantine room while raw materials approved room had the highest relative humidity of 33.33%. The results obtained for microbial loads showed that Escherichia coli, Staphylococcus aureus, Salmonella typhimurium and Pseudomonas aeruginosa recorded 0.00cfu/ml each. In contrast, the value obtained for total viable aerobic mesophilic bacteria plate count ranges from 0.00-28.67 cfu/ml and fungi range from 0.67-5.00 cfu/mL respectively. The significant difference was determined at p<0.05. However, the results obtained for the temperature, relative humidity and microbial loads were within the stated specifications. This shows that the temperature and relative humidity of the storage areas and the production room were controlled and well monitored in line with the current good manufacturing practice which will eventually positively impact the quality, marketability and stability of raw materials and drug products. Environmental monitoring of storage areas and production room should be highly encouraged in pharmaceutical industries to curb the menace of speedy degradation and loss of potency experienced in raw materials and finished pharmaceutical products.

Keywords:
Environmental, Microbiological, Monitoring, Storage areas, Production room

INTRODUCTION

The problem of degradation of both raw materials and finished pharmaceutical products (FPPs) has been of great concern to various stakeholders in pharmaceutical industries. This degradation caused by the storage and production environments affects the quality, safety and the potency of the drugs (EC, 2022). The environmental and microbiological conditions of where drugs are manufactured and stored must be balanced. In the same vein, the raw materials used for the production of drugs must be stored under the designated storage conditions to prevent degradation and loss of potency of active pharmaceutical ingredients (Oloninefa *et al.*, 2022). Temperature, relative humidity and microbial loads of the production and storage areas have been reported to have a great impact on raw materials and FPPs (Oloninefa *et al.*, 2022). The most critical factors involved in drug degradation as reported by Ansari (2017) and Kausar *et al.* (2013) are high temperature and relative humidity (RH).

Other factors such as air quality, time and production process characteristics can significantly impact the final quality and saleability of a product or batch of products (Ansari, 2017).Storage areas should be of sufficient capacity to allow for orderly storage of various categories of products, namely bulk and finished products, products in quarantine and released, rejected, returned or recalled products. Storage areas should be designed to ensure good storage conditions and clean, dry and maintained within acceptable temperature limits (Ansari, 2017; Kausar *et al.*, 2013). This study focuses on a one-year environmental and microbiological monitoring of storage areas and production room of a pharmaceutical industry from northern Nigeria.

MATERIALS AND METHODS

Study Area

The study covered one of the pharmaceutical industries located within northern Nigeria

Data Collection

The data for environmental and microbiological monitoring for storage areas (raw materials quarantine room, raw materials approved room, finished product quarantine room and finished product approved room) and production room were collected from one of the pharmaceutical industries in northern Nigeria. The data collected covered January to December 2022.

Data Analysis

The analysis of variance (ANOVA) of the data for environmental and microbiological monitoring for storage areas (raw materials quarantine room, raw materials approved room, finished product quarantine room, and finished product approved room) and production room was carried out using IBM SPSS Statistics Version 23. All data were expressed as mean ± standard error of the mean. The values with different superscripts along the same column were significantly different ($P < 0.05$).

RESULTS

The result of average monthly temperature obtained from the storage areas (raw materials quarantine room, raw materials approved room, finished product quarantine room and finished product approved room) and production room between January and December 2022 is presented in Table 1. The value average monthly temperature obtained from the storage areas are as follows: raw materials quarantine room (RMQR) had 21.10-29.27°C; raw materials approved room (RMAR) had 21.01-27.82°C; finished product quarantine room (FPQR) recorded 21.08-29.50°C while finished product approved room (FPAR) had values ranging from 23.20-29.23°C respectively. The value of monthly average temperature obtained from the production room ranges from 17.57-28.13°C (Table 1). However, the lowest temperature was 17.57°C and the highest was 29.50°C.

Furthermore, the result of average monthly relative humidity obtained from the storage areas (raw materials quarantine room, raw materials approved room, finished product quarantine room and finished product approved room) and production room between January and December 2022 is presented in Table 2. The value of average monthly relative humidity obtained from the storage areas are as follows: raw materials quarantine room (RMQR) had 11.11-30.33%; raw materials approved room (RMAR) had 11.67-33.33; finished product quarantine room (FPQR) had11.50-33.17% while finished product approved room (FPAR) had values ranging from 13.83-16.50% respectively. The value of average monthly relative humidity obtained from the production room ranges from 13.33-17.17% (Table 2). However, the lowest temperature was 11.11% while the highest was 33.33% (Table 2).

Table 3 shows the result of average monthly microbial load obtained from the production room between January and December 2022. There were no pathogenic bacteria obtained between January and December. The total viable aerobic mesophilic plate count recorded ranges from 0.00-28.67 cfu/ml while fungi had 0.67-5.00 cfu/ml (Table 3).The values with different superscripts are significantly different at $p<0.05$ (Tables 1-3).

Table 1: Average Monthly Temperature Obtained from the Storage Areas and Production Room in 2022

	Average Monthly Temperature (°C)											
Locations	**January**	**February**	**March**	**April**	**May**	**June**	**July**	**August**	**September**	**October**	**November**	**December**
RMQR	21.10 ±0.69^{a}	26.07 ±2.88^{a}	27.83 ±1.78^{a}	29.27 ±0.92^{c}	28.90 ±1.34^{b}	23.13 ±1.96^{a}	26.77 ±2.59^{a}	26.60 ±0.66^{a}	27.32 ±1.03^{b}	28.90 ±0.49^{b}	22.90 ±0.96^{a}	28.37 ±2.34^{b}
RMAR	21.01 ±1.95^{a}	26.45 ±1.31^{a}	27.82 ±2.06^{a}	25.17 ±1.63^{b,c}	25.83 ±2.09^{a,b}	27.13 ±2.35^{a}	26.77 ±2.59^{a}	26.88 ±0.95^{a}	26.28 ±0.69^{b}	27.80 ±0.83^{b}	22.07 ±0.91^{a}	27.27 ±0.68^{b}
FPQR	25.62 ±0.69^{a,b}	27.33 ±2.79^{a}	27.10 ±2.06^{a}	21.08 ±1.88^{a,b}	22.08 ±1.61^{a}	28.68 ±0.98^{a}	27.33 ±2.42^{a}	29.50 ±2.91^{a}	27.57 ±2.29^{b}	29.10 ±0.40^{b}	23.37 ±0.88^{a}	27.57 ±0.58^{b}
FPAR	23.48 ±0.82^{a,b}	26.67 ±0.46^{a}	27.57 ±2.29^{a}	25.87 ±2.25^{b,c}	26.52 ±0.51^{a,b}	28.17 ±1.64^{a}	26.75 ±0.46^{a}	27.33 ±2.24^{a}	27.13 ±2.04^{b}	29.23 ±0.64^{b}	23.20 ±0.78^{a}	27.13 ±0.58^{b}
Production Room	25.9 0±1.98^{b}	23.50 ±1.82^{a}	23.23 ±1.58^{a}	17.57 ±2.16^{a}	28.13 ±1.58^{b}	23.40 ±1.86^{a}	21.55 ±0.86^{a}	24.13 ±2.34^{a}	21.53 ±0.60^{a}	21.83 ±0.87^{a}	23.32 ±0.90^{a}	21.02 ±0.71^{a}

Results represent mean ± standard error of the mean of triplicate determination. Values with the same superscript in the same column are not significantly different at p<0.05
KEY: RMQR – Raw Material Quarantine Room, **RMAR** – Raw Material Approved Room, **FPQR** – Finished Product Quarantine Room and **FPAR** – Finished Product Approved Room

In-House Specifications:
RMQR: Alert Limit: 42.88°C; Action Limit: 48.82°C, **RMAR**: Alert Limit: 30.14°C; Action Limit: 31.06°C, **FPQR**: Alert Limit: 33.57°C; Action Limit: 35.61°C, **FPAR**: Alert Limit: 36.15°C; Action Limit: 39.24°C and **Production Room**: Alert Limit: 26.61°C; Action Limit: 27.41°C

Table 2: Average Monthly Relative Humidity Obtained from the Storage Areas and Production Room in 2022

	Average Monthly Relative Humidity (%)											
Locations	**January**	**February**	**March**	**April**	**May**	**June**	**July**	**August**	**September**	**October**	**November**	**December**
RMQR	11.11 ±0.38^{a}	12.82 ±0.32^{a}	13.24 ±0.91^{a}	14.14 ±0.92^{a}	25.50 ±2.36^{b}	30.33 ±2.73^{c}	24.50 ±2.52b	28.00 ±4.36^{b}	25.53 ±5.16^{b,c}	28.58 ±3.15^{b,c}	22.60 ±1.23^{b}	11.17 ±0.60^{a}
RMAR	17.70 ±2.14^{b}	23.30 ±1.65^{b}	26.00 ±1.76^{b}	25.50 ±1.26^{b}	27.00 ±2.31^{b}	23.67 ±0.88^{b}	24.50 ±2.52b	33.33 ±2.20^{b}	21.33 ±1.10^{a,b}	23.00 ±1.15^{b}	24.17 ±1.64^{b}	11.67 ±1.20^{a}
FPQR	24.20 ±2.08^{c}	27.64 ±1.02^{b}	25.67 ±1.88^{b}	31.00 ±1.04^{c}	29.63 ±0.47^{b}	28.29 ±0.60^{b,c}	30.52 ±0.59b	29.17 ±0.93^{b}	31.83 ±1.09^{c}	33.17 ±1.59^{c}	14.83 ±1.36^{a}	11.50 ±0.76^{a}
FPAR	14.50 ±1.04^{a,b}	15.33 ±2.03^{a}	16.33 ±0.88^{a}	16.00 ±1.73^{a}	16.33 ±0.44^{a}	14.50 ±1.61^{a}	15.43 ±1.90a	15.17 ±0.73^{a}	16.00 ±1.76^{a}	13.83 ±0.73^{a}	14.83 ±1.59^{a}	16.50 ±3.40^{a}
Production Room	17.00 ±1.15^{b}	16.00±2.02^{a}	15.50 ±1.04^{a}	17.17 ±1.59^{a}	13.33 ±1.20^{a}	13.50 ±0.29^{a}	13.83 ±2.08a	13.50 ±0.58^{a}	14.62 ±0.92^{a}	13.89 ±2.06^{a}	15.13 ±1.68^{a}	16.33 ±3.28^{a}

Results represent mean ± standard error of the mean of triplicate determination. Values with the same superscript in the same column are not significantly different at p<0.05
KEY: RMQR – Raw Material Quarantine Room, **RMAR** – Raw Material Approved Room, **FPQR** – Finished Product Quarantine Room and **FPAR** – Finished Product Approved Room

In-House Specifications:
RMQR: Alert Limit: 97.56%RH; Action Limit: 114. 63%RH, **RMAR**: Alert Limit: 87.49%RH; Action Limit: 100. 31%RH, **FPQR**: Alert Limit: 99.97%RH; Action Limit: 118. 11%RH, **FPAR**: **Alert Limit**: 103.06%RH; Action Limit: 123. 84%RH and **Production Room**: Alert Limit: 56.01%RH; Action Limit: 57.01%RH

Table 3: Average Monthly Microbial Load Obtained from the Production Room in 2022

	Average Monthly Microbial Load (cfu/ml)											
Parameters	**January**	**February**	**March**	**April**	**May**	**June**	**July**	**August**	**September**	**October**	**November**	**December**
[1]Pathogenic bacteria	0.00 ±0.00[a]	0.00 ±0.00[a]	0.00 ±0.00[a]	0.00 ±0.00[a]	0.00 ±0.00[a]	0.00 ±0.00[a]	0.00 ±0.00[a]	0.00 ±0.00[a]	0.00 ±0.00[a]	0.00 ±0.00[a]	0.00 ±0.00[a]	0.00 ±0.00[a]
[2]TVAMBPC	0.00 ±0.00[a]	25.00 ±7.23[b]	11.00 ±0.58[b]	6.67 ±0.33[c]	28.67 ±9.33[b]	0.33 ±0.33[a]	1.00 ±0.58[a,b]	2.67 ±1.45[a]	1.67 ±0.67[a,b]	3.00 ±0.58[c]	6.00 ±2.00[b]	1.67 ±0.33[b]
[3]Fungi	2.00 ±1.15a	1.00 ±0.00[a]	1.00 ±0.00[a]	5.00 ±0.00[b]	0.67 ±0.33[a]	1.00 ±0.00[b]	1.67 ±0.33[b]	2.33 ±0.33[a]	2.67 ±0.67[b]	1.67 ±0.33[b]	1.00 ±0.00[a]	0.67 ±0.33[a]

Results represent mean ± standard error of the mean of triplicate determination. Values with the same superscript in the same column are not significantly different at $p<0.05$

KEY: TVAMBPC –Total Viable Aerobic Mesophilic Bacteria Plate Count

LIMITS:

1 - B. P & In-house Specifications: Nil

2 - B. P: ≤100 cfu/ml; **In-house Specifications:** Wet Season: ≤80 cfu/ml; Dry Season: ≤60 cfu/ml

3 - B. P: ≤10 cfu/ml; **In-house Specifications:** Wet Season: ≤8 cfu/ml; Dry Season: ≤6 cfu/ml

DISCUSSION

The results obtained from environmental monitoring of storage areas and production room fell within the stated in-house specifications. The results were in agreement with the reports of Oloninefa *et al*. (2022) and Kumar and Jha (2016) that opined that the quality and control of microbial load of raw materials and finished pharmaceutical products (FPPs) are guarantee when the temperature and relative humidity of storage areas and the microbial load of production room are controlled and regulated as per the stated specifications. Monitoring of the temperature and relative humidity of storage areas such as raw materials quarantine room, raw materials approved room, finished product quarantine room and finished product approved room assist in preventing quick degradation and enhance the stability of the raw materials and FPPs (Oloninefa *et al*., 2022; Ansari, 2017). The results of microbial load, temperature and relative humidity from the storage areas and production room falling within the in-house specifications will contribute immensely to the stability of both the raw materials and the FPPs as reported by Kumar and Jha (2016) and GCC (2018).

Furthermore no pathogenic bacteria recorded from the production room and the total bacteria viable aerobic mesophilic bacteria count and fungi count obtained were within the stated in-house specifications. This suggests high compliance to the current good manufacturing practice (cGMP). This also will go a long way to prevent the contamination of the drug products inside the production room (Oloninefa *et al*., 2022; Mukhtar *et al*., 2019; Noor *et al*., 2015). Bajaj *et al*. (2012) and Kiron *et al*. (2011) reported that to show great concern with respect to the welfare of the end users of FPPs, good storage conditions must be maintained since they have great implications on the quality of the drug product.Sultana& Mohammed (2018) and Nicolas *et al*. (2021) opined that temperature and relative humidity are critical factors that must be controlled in manufacturing facilities to produce quality products, maintain the stability and marketability of the drug products.

WHO (1996) reported that the stability of drug products depends mainly on environmental factors such as temperature and relative humidity and other product-related factors such as chemical and physical properties of the active pharmaceutical ingredients (APIs) and excipients. Therefore, controlling and maintaining the temperature and relative humidity of the storage areas and production room within the designated specifications is very important as this will guarantee the storage and quality of temperature-sensitive products (WHO, 2011).

CONCLUSION

The results obtained from the environmental monitoring of storage areas and production room showed that there was a compliance with stated specifications. This will go a long way to reduce quick degradation, promote stability and enhance the quality of raw materials and the finished pharmaceutical products (FPPs). The patronage and marketability of the FPPs will also be enhanced. Therefore, environmental monitoring of the storage areas and the production room in pharmaceutical industries should be well encouraged and maintained in line with the guidelines stated in the current good manufacturing practice (cGMP) and stated in-house specifications by all stakeholders in pharmaceutical industries.

CONFLICT OF INTEREST

There is no conflict of interest among the authors.

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