MAPPING OF MEDICINES STORAGE CONDITIONS IN WAREHOUSES AND RETAIL OUTLETS IN TANZANIA

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MAPPING OF MEDICINES STORAGE CONDITIONS IN WAREHOUSES AND RETAIL OUTLETS IN TANZANIA

By

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A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Masters of Pharmacy in Quality Control and Quality Assurance of Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The undersigned certify that they have read and hereby recommends for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled **Mapping of medicines storage conditions in warehouses and retail outlets in Tanzania,** in (Partial) fulfillment of the requirement for degree of Master of Pharmacy of Muhimbili University of Health and Allied Sciences.

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DECLARATION AND COPYRIGHT

I, **Makala Erasto Nzinza**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other university for similar or any other degree award.

Signature……. Date……

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Many thanks to the Supply Chain Management System for the donation of the temperature and humidity loggers which made this study possible.

DEDICATION

With love and affection, this work is dedicated to my sons Amos and Elias my daughter Agnes, my wife Rachel and my parents for supporting me during my studies.

ABSTRACT

Background: As global warming is now widely accepted as a reality, temperature and humidity are likely to become ever more of a problem in warehouses and outlets as far as storage conditions are concerned. Hence storage conditions mapping becomes of critical importance in order to ensure that the great debate among different stakeholders on whether the prescribed labelled storage conditions for medicines can be achieved in the real market supply chain facilities

Study Objectives: To assess temperature and relative humidity storage conditions in Tanzania for the Good Storage Practice of medicines according to the International Committee on Harmonization (ICH). The information obtained from this study will help to advice the regulatory Authority on the stability requirements and letting for Tanzania.

Methods: The study involved selected warehouses and retail outlets. These were six public warehouses and six private medicine outlet facilities which include medical stores department warehouses, Government hospital warehouses/pharmacies and community warehouses/pharmacies. Data collection involved a site visit to mount digital temperature and humidity data loggers, which were programmed to automatically collect, and record twice per day i.e mid-day at 12:10 hrs and mid-night at 00:10 hrs conditions over a period of one year. In the current study, the storage conditions were determined through calculation of the mean kinetic temperature and the arithmetic mean relative humidity (RH) formula. The parameters were collected from daily point temperatures and humidity in six different geographic zones of Tanzania mainland. The data have been analyzed with the program prepared in the Microsoft Excel 2007 using the MKT formulae; and data presented in tables and graphs. The analysis for temperature and relative humidity data were calculated by using the mean kinetic temperature and arithmetic mean formula respectively.

Results: A total of 8760 data reading each for temperature and relative humidity were collected for one year. The overall Mean Kinetic Temperature for Tanzania mainland calculated value was 25.63 ^{o}C and the arithmetic mean relative humidity

calculated was 60.2%. The highest temperature value was recorded in the Coastal zone (34.1 ^{o}C) and lowest was in the Southern highland zone (12.05 ^{o}C). The highest relative humidity value was in the Coastal zone (89.0%) and lowest was in Southern highland zone (25.0%).

Conclusion: Tanzania which covers a large area records a variation of climate, example in Northern zone and Southern highland zone the temperature is much lower compared to the Coastal zone. The storage facilities in Tanzania do comply with the Good Storage Practice of medicines according to the International Committee on Harmonization (ICH) with respect to temperature and relative humidity. The data suggest Tanzania fits well in climatic zone IVb 30 °C ± 2 °C/75% RH ± 5% RH and Zone II (25 ± 2^{o}C/60 ±5%) according to ICH guidelines, in principle this argument holds only and only if the facility is fitted with air-conditioning. However, with the current requirement one puts low risk by considering the worst case scenario while on the other hand it would mean some good quality medicine are wasted as a consequence of underestimated shelf life. The economic loss resulting from this remains undetermined.

Recommendation: The study recommends mapping of storage conditions from facilities not fitted with air-conditioning to see whether they will also comply with ICH conditions

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LIST OF ABBREVIATIONS/ACRONYMS

ASEAN	Association of South East Asian Nations
^{O}C	Degrees Celsius
e	Base of natural logarithm
EC	European Community
$\triangle H$	Activation Energy
H	Highland
Hrs	Hours
ICH	International Committee on Harmonization
ln	natural logarithm
MKT	Mean Kinetic Temperature
MSD	Medical Stores Department
MUHAS	Muhimbili University of Health and Allied Sciences
PC	Personal Computer
R	Universal gas Constant
RH	Relative Humidity
SCMS	Supply Chain Management System
TFDA	Tanzania Food and Drugs Authority
T_K	Mean Kinetic Temperature in Kelvin
USA	United States of America
USP	United States Pharmacopoeia
WHO	World Health Organization

CHAPTER ONE

1.1 INTRODUCTION

1.1.1 Background

Good quality medicines are a prerequisite to successful treatment. The quality assurance of medicines begins in the early stages of product development to manufacturing of the finished pharmaceutical products [(1)]. It does not end up here as continuation into medicine storage and distribution supply chain, is equally paramount to maintenance of adequate product quality. Good quality manufactured medicines can lose potency and become substandard [(2)] because of poor storage conditions during transportation, in warehouses, retail outlets and even in households during use. This degradation may lead to medicines becoming toxic or inactive[(1)]. Poor quality drug preparations may lead to adverse clinical results both in terms of low efficacy and encouraging drug resistance [(3,4)].

High temperatures above 30^{o}C and relative humidity (RH) of 75% are the most important factors, which influence medicine degradation kinetics. Although stability testing at high temperatures and relative humidity are mandatory in medicine development process, this should not exclude quality monitoring of the medicines.

1.1.2 Stability of drug products

Almost all drug products undergo physicochemical degradation. The extent of the degradation depends on many factors, such as storage conditions, product stability and packing materials. One negative outcome of drug product degradation is the failure of the preparation to maintain the required potency over the shelf life. Moreover, various ingredients of the drug product may undergo chemical interactions through exposure to high temperatures and humidity. These interactions could affect significantly the physical state of the drugs and may generate toxic substances[(4)].

The effect of high relative humidity on the stability of medicinal products during storage and distribution is relatively insignificant. However, humidity can have a deleterious effect on the strength of secondary cardboard packaging. Cartons stacked in environments where the relative humidity is high (such as in cold stores or in

refrigerated transport) can become softened and collapse, exposing their contents to the risk of damage from physical shock [5].

1.1.3 General storage conditions and stability studies

The stability of medicines distributed and used in hot and humid climates can pose serious problems, but stability studies and guidelines usually refers to temperate climates and therefore may not be relevant in extreme climatic conditions [6, 7, 8].

The storage conditions and the extent of stability studies selected should sufficiently address storage, shipment and subsequent use of a particular medicine with due regard to the climatic conditions in which the same is intended to be marketed [9].

Storage condition tolerances are usually defined as the acceptable variations in temperature and relative humidity of storage facilities for stability studies [10]. The equipment used should be capable of controlling the storage conditions within the ranges. Long-term (real time) and accelerated storage conditions for pharmaceutical products can be observed as in a climatic zone IVb where Tanzania is included as shown in Table 1.1.1[11].

Table 1.1.1:Study of storage condition minimum period covered by data at submission in climatic zone IVb

Study	Storage Condition	Minimum time period covered
Long term	30 °C ± 2 °C/75% RH ± 5% RH	12 months
Accelerated	40 C ± 2 °C/75% RH ± 5% RH	6 months

1.1.4 Global storage Conditions and Climatic Zones

Globally, storage conditions is still an issue to manufacturers when sending labeled packaging materials with instructions for climate zone II to markets in climates of tropical zones of IVa and IVb[12]. This is because they do not find it necessary to spend money on instituting relevant packaging and conducting stability studies. The International Conference on Harmonization (ICH) and the World Health

Organization (WHO) recommend that storage for medicines in climate zone IVb should not be above 30°C[12].

ICH stability guidelines apply to climate zones I and II, whereas WHO lists requirements for climate zones I–III, IVa, and IVb. The standard climatic zones for use in pharmaceutical product stability studies are shown in Table 1.1.2[13, 14] shows storage conditions for different climatic zones while Table 1.1.3 list the components in the long term testing conditions[8, 9].

Table 1.1.2: Climatic Zones

Zone	**Type of Climate**
Zone I	Temperate zone
Zone II	Mediterranean/subtropical zone
Zone III	Hot dry zone
Zone IVa	Hot humid/tropical zone
Zone IVb	Hot/higher humidity

Table 1.1.3: Long Term Testing Conditions

Climatic Zone	**Temperature**	**Humidity**	**Minimum Duration**
Zone I	21ºC ± 2ºC	45% RH ± 5% RH	12 Months
Zone II	25ºC ± 2ºC	60% RH ± 5% RH	12 Months
Zone III	30ºC ± 2ºC	35% RH ± 5% RH	12 Months
Zone IVa	30ºC ± 2ºC	65% RH ± 5% RH	12 Months
Zone IVb	30ºC ± 2ºC	75% RH ± 5% RH	12 Months
Refrigerated	5ºC ± 3ºC	-	12 Months
Frozen	-15ºC ± 5ºC	-	12 Months

Other countries accept drugs developed at much lower standards to circulate in their markets. One example is India where most of its products are labeled 'store below 25^{o}C as the nationally accepted standard irrespective of the fact that medicines are frequently sold in drug outlets openly without air conditioners and / or refrigerators [15].

The International Conference on Harmonization and the World Health Organization have argued for many years on the question of storage conditions in ASEAN countries, and came up with climate zone IVb accelerated testing at 40^{o}C/75% relative humidity. The recommended storage condition for medicines that meets the requirements for climate zone IVb should not be above 30^{o}C. However, there is no storage instruction for relative humidity.

This recommended storage instruction is sometimes not clear to patients because they can even store tablets in the refrigerators during hot conditions because to them there is no limit as to how low the temperatures are supposed to go. But storage in refrigerators is accompanied with exposure to high humidity leading to fungal growth on the tablets.

1.1.5 Medicine Storage procedure and instructions

Pharmaceutical products must be stored under conditions which minimize deterioration, contamination and damage. They should also be stored under conditions compatible with their recommended temperature and humidity storage requirements. The appropriate temperatures for materials labeled "store in refrigerator" should be between 2^{o}C and 8^{o}C and those labeled "store in freezer" between -5^{o}C and -20^{o}C[16] In the absence of more stringent storage requirements, pharmaceutical products and raw materials should be stored on the average below 25^{o}C **to** 30^{o}C[16].

1.1.6 Literature review

Storage conditions for stability testing changes according to the climatic condition of the particular area of the study. According to the study carried out [17] in EC, Japan and USA, a lot of efforts have been undertaken to harmonize the requirements for the investigation of the stability of drug substances and drug products. The results of these investigations are used to assign labeling, which properly reflects the stability

of the substances/products under the climatic conditions encountered in the region of distribution. According to this study, the EC, Japan and the USA may be practically assigned to a region for which there is an annual mean kinetic temperature of up to 25°C.

In fact, the climatic study indicates that 25°C/60%RH is generally well above the mean kinetic temperature for the 35 major European, Japanese and American cities covered in the study. In addition, the mean kinetic temperature encompasses the data in warehouses as well as measured seasonal and daily fluctuations up to and above the extreme temperature of 30°C allowed by the USP definition of controlled room temperature. Based upon the above, it can therefore be concluded that long term controlled room temperature labeling for the USA, Japan and the EC can be accurately assigned by applying storage condition of 25°C/60%RH [18].

Moreover literature survey reported a successful data based on the hottest and the most humid place in each country or region identified to reflect the worst case for the specific region. Long-term stability testing condition recommended for each selected country, related to the worst case for each region and the safety margins [18].

Literature further reveals that storage conditions for stability testing in Brazil regions were derived and examined comparatively with the guidelines of the World Health Organization (WHO) and regulatory bodies[4]. The storage conditions were derived from the calculated values of the mean kinetic temperature and the relative humidity (RH). Some regions present RH values higher than 80%, giving support to the concerns of the WHO, indicating the necessity for revision of existing guidelines on stability testing mainly for very hot and humid regions[5]. Controlled Room Temperature is a temperature maintained thermostatically that encompasses the usual and customary working environment of 20°C to 25°C that results in a mean kinetic temperature calculated to be not more than 25°C; and that allows for excursions between 15°C and 30°C that are experienced in pharmacies, hospitals, and warehouses. Provided the mean kinetic temperature remains in the allowed range, transient spikes of up to 40°C are permitted as long as they do not exceed 24 hours [15]. Furthermore disclosed that poor quality at the endpoint is often due to poor initial quality rather instability of the product[19].

1.2 STATEMENT OF THE PROBLEM

As global warming is now widely accepted as a reality, temperature and humidity are likely to become ever more of a problem in warehouses and outlets as far as storage conditions are concerned. Statistics demonstrate that temperatures above 25°C have been the biggest challenge for those who are responsible for the storage of pharmaceutical products [20]

Due to high temperatures and humidity, good quality manufactured medicines may lose potency and become substandard because of poor storage conditions in warehouses, retail outlets and even in households. This may lead to medicines becoming toxic or inactive.

1.3 RATIONALE

Storage condition mapping is of critical importance in order to ensure that the debate among different stakeholders on whether the prescribed storage labeling conditions for medicines are achievable in the real supply chain facilities.

The acquired information on medicines storage can be used to make important recommendations to manufacturers on storage conditions labeling in Tanzania.

1.4 RESEARCH QUESTIONS

i. What are the required storage conditions in Tanzania from this study?

ii. Is there any difference of storage conditions between the current used and that of the findings for stability testing?

iii. Which zone of Tanzania and month in a year has the highest mean kinetic temperature/mean relative humidity?

1.5 OBJECTIVES

1.5.1 Broad Objective

To assess temperature and relative humidity storage conditions in Tanzania with respect to compliance to the Good Storage Practice of medicines according to the International Committee on Harmonization requirement of 30°C/75%.

1.5.2 Specific objectives

i. To map temperature and relative humidity at the selected warehouses, hospital pharmacies and private community pharmacies.

ii. To determine whether the storage conditions required in Tanzania in accordance to ICH at zone IVb (hot and very humid) are achievable.

iii. To determine the mean kinetic temperature and arithmetic mean relative humidity for Tanzania.

CHAPTER TWO

2.1 METHODS

2.1.1 Study area

The assessment mainly focused on the storage conditions in warehouses and retail outlets at six selected public warehouse and six private medicine facilities. These included medical stores department warehouses, government hospital warehouses /pharmacies and community warehouses/pharmacies as shown in Table 2.1.1 and map figure 2.1.1.

Table 2.1.1: Sampling site in zones of Tanzania

S/No.	Zone	Site	Name of Site	Type
1	Coastal zone	A	MSD Headquarter warehouse-Dar es Salaam	Public
		A1	Action Medeor warehouse-Dar es Salaam	Private
		B	Mwanacoco pharmacy-Dar es Salaam	Private
2	Central zone	A	MSD Warehouse-Dodoma	Public
		B	Blue pharmacy-Dodoma	Private
3	Lake Zone	A	Bugando Hospital Warehouse-Mwanza	Public
		B	Mkuyuni pharmacy-Mwanza	Private
4	North Zone	A	Tanzania Pharmaceutical Industry Warehouse-Arusha	Public
		B	Nile pharmacy-Arusha	Private
5	South highland zone	A	MSD Warehouse-Mbeya	Public
		B	Bhojan pharmacy-Mbeya	Private
6	West zone	B	Kitete Region hospital pharmacy-Tabora	Public

Where site ‘A’ and ‘A1’ are whole seller (public or private warehouse) and “B” is retail outlet (community or hospital pharmacy).

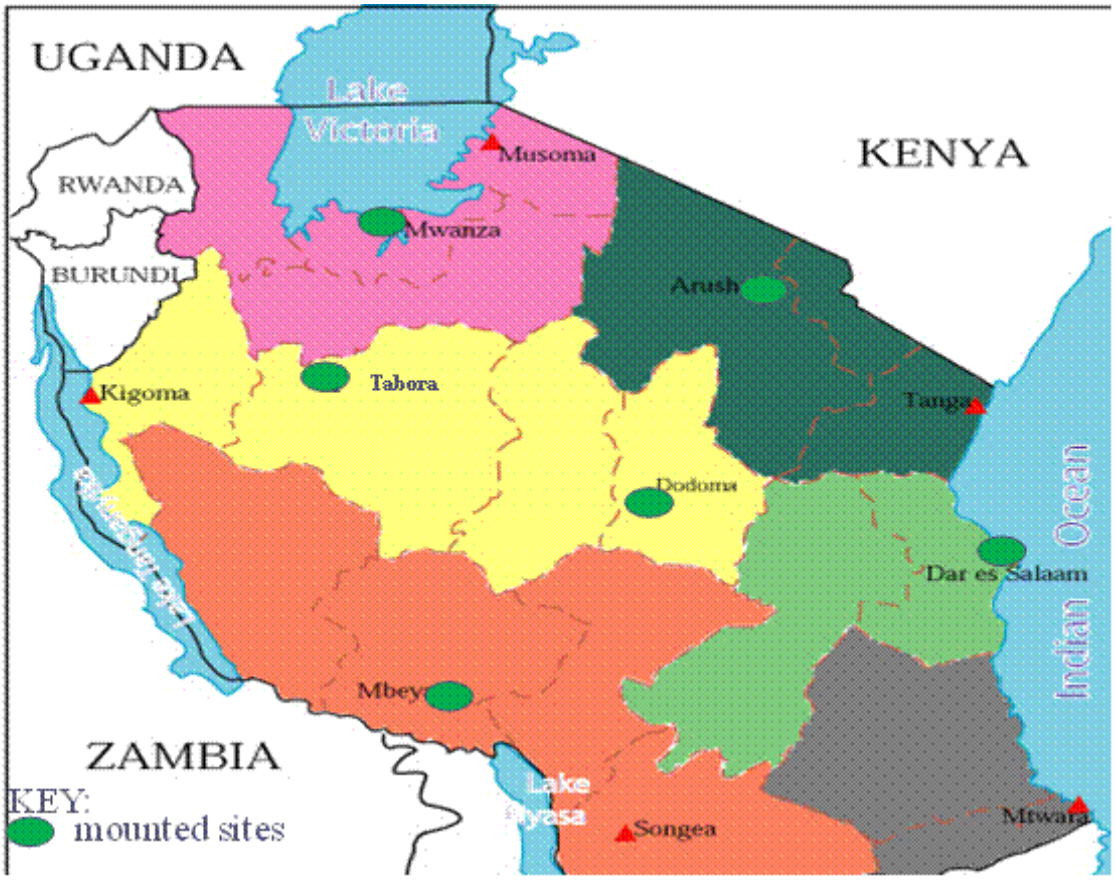

Figure 2.1.1: Mapping Sites in Tanzania

2.1.2 Sampling Method for the Facilities

A simple random sampling was used to obtain the facilities. In this case, one facility was selected from each region. A list of facilities in each region was obtained, each facility was given a number and these numbers were written on small pieces of paper. All the papers were put in a box, after which the box was shaken to ensure randomization. Then, number of papers representing each region were taken out of the box and recorded. Data from these facilities was used as representative of storage conditions in the respective zone.

2.1.3 Sample Size

The sample size was drawn from a targeted population/area. This was done in six zones in Tanzania where twelve facilities were selected for automatic storage

conditions data collections in six public and six private medicine facilities. The sample size estimated was 8760 for temperature and 8760 readings for relative humidity samples.

2.1.4 Study design

The design of study was descriptive longitudinal

2.1.5 Period of the study

The study was conducted from August 2012 to July 2013.

2.1.6 Pre-testing of data collecting Tools

The data collection tools (data loggers) were tested as a pilot study.

2.1.7 Ethical Clearance.

Ethical clearance was granted by the Ethical Review Committee of the Muhimbili University of Health and Allied Sciences (MUHAS). The researcher asked permission to collect data from MSD headquarter, Government hospital and in some community pharmacies visited.

2.1.8 Equipments

Digital data loggers (ibutton devices) were factory programmed to meet the accuracy specifications as defined in their corresponding data sheet. All device parameters for temperature and humidity accuracy were guaranteed for 1 (one) year under Maxim standard terms and conditions, with the condition they have been properly handled and used within all operating condition ranges specified in the data sheet.

The data loggers determined the current temperature by measuring the inherent physical properties of their onboard integrated circuits. Exhaustion of the internal lithium battery can be caused by age, temperature and sampling rate.

The following were the procedures required for installation, setting and exporting or downloading of data from the thermochron /hygrochronibutton devices [(21)].

a. The communication made in the computer with 64-bit operating system of PC or laptop.

b. In order to run this programme, java software must be installed; note application gives detailed installation instructions for PC or laptop using Windows 7, Window vista or Window XP operating system.

c. One Wire Viewer and 1-Wire driver was convenient demonstration software program that allows users to easily read from and write ibuttons with a window based PC or laptop.

d. After installation was done, all parameters were set into ibutton device to start the mission of collecting temperature and relative humidity in the respective sites where they were taken automatically.

After the period set for data collection all data were exported/ downloaded from ibutton device into an excel spreadsheet for statistical analysis.

2.1.9 Sampling technique and Data Collection

The methodology involved a site visit to mount digital temperature and humidity data loggers that automatically collect and record data twice per day i.e. midday at 1210hrs and midnight at 0010hrs over a period of one year. The sites for warehouses and pharmacies indicated in Table 2.1.1 above were picked from six zones of Tanzania where each zone had almost different weather conditions and thereafter at least one or more site facility(ies) were selected for data collection.

2.1.10 Data analysis

The data was downloaded through program installed in PC at the end of the year of research. Analysis was made by calculating the Mean Kinetic Temperature (MKT) for temperature and Arithmetic Mean for Relative Humidity data.

Mean Kinetic Temperature is defined by the USP as "the single calculated temperature at which the total amount of degradation over a particular period is equal to the sum of the individual degradations that would occur at various temperatures. Thus, MKT may be considered as an isothermal storage temperature that simulates the non-isothermal effects of storage temperature variations. It is not a simple arithmetic mean. MKT is calculated from temperatures in a storage facility. In other words, it is a single value that is used to represent the effect of a series of temperatures measured over a period of time. The importance to the pharmaceutical

industry is that, it may be a single, or a few excursions over time from the established range may not result in damaged product [22].

The equation 1 below used to calculate the MKT is:

$$T_K = \frac{\frac{\Delta H}{\Re}}{-\ln\left(\frac{e^{\frac{-\Delta H}{\Re T_1}} + e^{\frac{-\Delta H}{\Re T_2}} + \ldots e^{\frac{-\Delta H}{\Re T_n}}}{n}\right)}$$

Where:

T_K is the mean kinetic temperature in Kelvins

ΔH is the activation energy (83.144 kJ/mole

R is universal gas constant (8.3144×10^{-3} kJ/mole/degree)

T_1 to T_n are the temperatures at each of the sample points in Kelvin's

n is the total number of storage temperatures recorded during the annual observation period

e is the base of the natural logarithm,

The above equation is valid only when the temperature readings are taken at the same interval. A more general form for the above equation 1 can be expressed as:

$$T_K = \frac{\frac{\Delta H}{\Re}}{-\ln\left(\frac{t_1 e^{\frac{-\Delta H}{\Re T_1}} + t_2 e^{\frac{-\Delta H}{\Re T_2}} + \ldots t_n e^{\frac{-\Delta H}{\Re T_n}}}{t_1 + t_2 + \ldots t_n}\right)}$$

Where:

to t_n are time intervals at each of the sample points

When $t_1 = t_2 = \ldots = t_n$, this equation 2 was reduced to the equation 1[23, 24, 25]. The MKT can be easily calculated through the software calculator using the following website; www.compendiallearning.com/.../launch.htm but mean kinetic temperature was calculated by the MKT formula programmed in the Microsoft Excel 2007.

MKT gives a far better representation of the effects of temperature change on sensitive materials such as pharmaceuticals and food products during storage and distribution. In many instances it can be shown that the 'shelf life' of sensitive materials is directly related to the MKT. Mean Kinetic Temperature can be calculated from a series of temperatures. It differs from other means (such as a simple numerical average or arithmetic mean) in that higher temperatures are given greater weight in computing the average. This weighting is determined by a calculation giving the natural logarithm of the temperature value. The key to the MKT calculation is that it gives increased weighting to higher temperature excursions than normal arithmetic methods, recognizing the accelerated rate of thermal degradation of materials at higher temperatures[26]. This is done if mean temperature is calculated and the difference between two temperatures is greater than five (5) then the MKT is used for calculation instead of arithmetic mean temperature. Example arithmetic mean for 20^{o}C and 40^{o}C is 30^{o}C while mean kinetic temperature is 34.4^{o}C [22].

CHAPTER THREE

3.0 RESULTS AND DISSCUSION

3.1 RESULTS

A total of 8760 samples for temperature and 8760 samples of relative humidity were collected from August 2012 to July 2013. The overall Mean Kinetic Temperature calculated was 25.63^{o}C and the arithmetic mean for relative humidity was 60.2%. The variation in the temperatures and relative humidity data for the country zones were observed.

3.1.1 Climatic diversity between the Tanzanian regions

The temperature values for the six zones are shown in Table 3.1.1 below. The lowest temperature values were recorded in the Southern highland zone followed by Western zone and Northern zone. The highest temperature values were recorded in the Coastal zone followed by Central zone and Lake zone. The highest Mean Kinetic Temperature was calculated for the Coastal zone followed by the Western zone and Central. The lowest Mean Kinetic Temperature was calculated for the Southern highland zone followed by the Northern zone and Lake zone.

Table 3.1.1: Lowest, Highest temperature data and Mean Kinetic Temperature

Item	Central Zone	Coastal Zone	Lake Zone	Southern H. zone	Western Zone	Northern Zone
Lowest Temperature (^{o}C)	20.1	23.1	19.1	12.05	17.6	17.6
Highest Temperature (^{o}C)	31.1	34.1	29.6	27.1	31.1	28.6
MKT (^{o}C)	25.9	28.2	24.6	21.19	27.3	24.4
Overall MKT (^{o}C)	25.63					

3.1.2 Relative Humidity changes with time period and regions

The relative humidity values for the six zones are shown in Table 3.1.2 below. The highest relative humidity values were recorded in the Coastal zone followed by Lake zone and Northern zone. The lowest relative humidity values were recorded in the Western zone followed by Northern zone and Southern highland zone. The lowest arithmetic mean for relative humidity was calculated for the Western zone followed by the Central zone and Northern zone. The highest arithmetic mean for relative humidity was calculated for the Coastal zone followed by the Southern highland zone and Lake zone.

Table 3.1.2: Lowest, Highest Relative Humidity and arithmetic Mean

Item	Central Zone	Coastal Zone	Lake Zone	Southern H. Zone	Western Zone	Northern Zone
Lowest Relative Humidity (%)	35.7	41.8	37.4	32.5	25.0	32.2
Highest Relative Humidity (%)	79.0	89.0	82.4	72.2	66.7	80.1
Arithmetic Mean (%)	53.9	66.0	61.6	63.54	47.5	59.4
Overall Arithmetic Mean (%)	60.2					

The figure 3.1.1 below shows the calculated Mean Kinetic Temperature and relative humidity in the central zone. Mean Kinetic Temperature showed to be high in December, January and February. The calculated relative humidity was high in April, January and February.

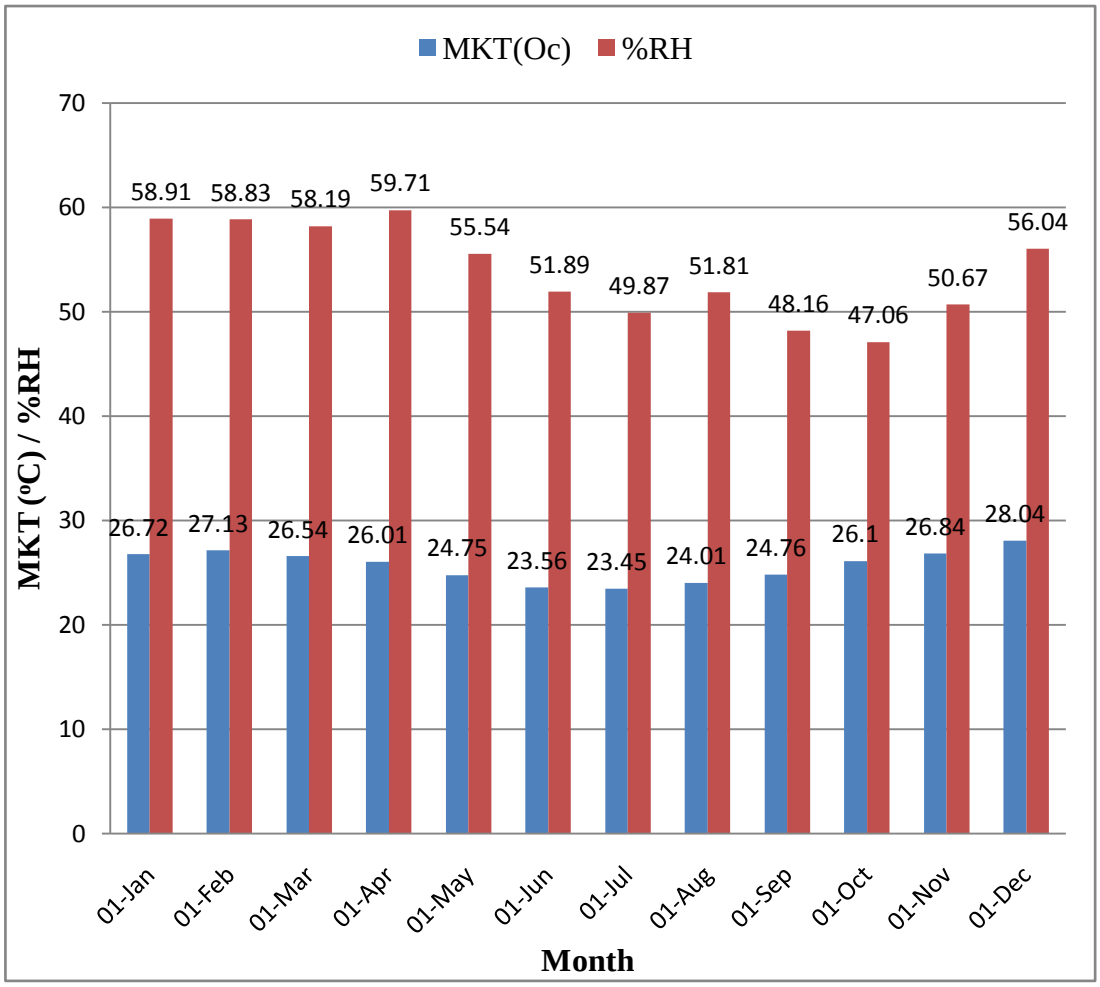

Figure 3.1.1: Trends of MKT/RH in Central Zone for the year 2012/2013

In contrast to the Mean Kinetic Temperature calculated for the Central zone, that temperature in the Coastal zone was high in almost all months of the year (figure 3.1.2). The highest temperature was observed in February, December and January and the lowest temperature in July and therefore the range was 3.11 ^{o}C.

At the same time relative humidity in this region was found to be high in April, March and January.

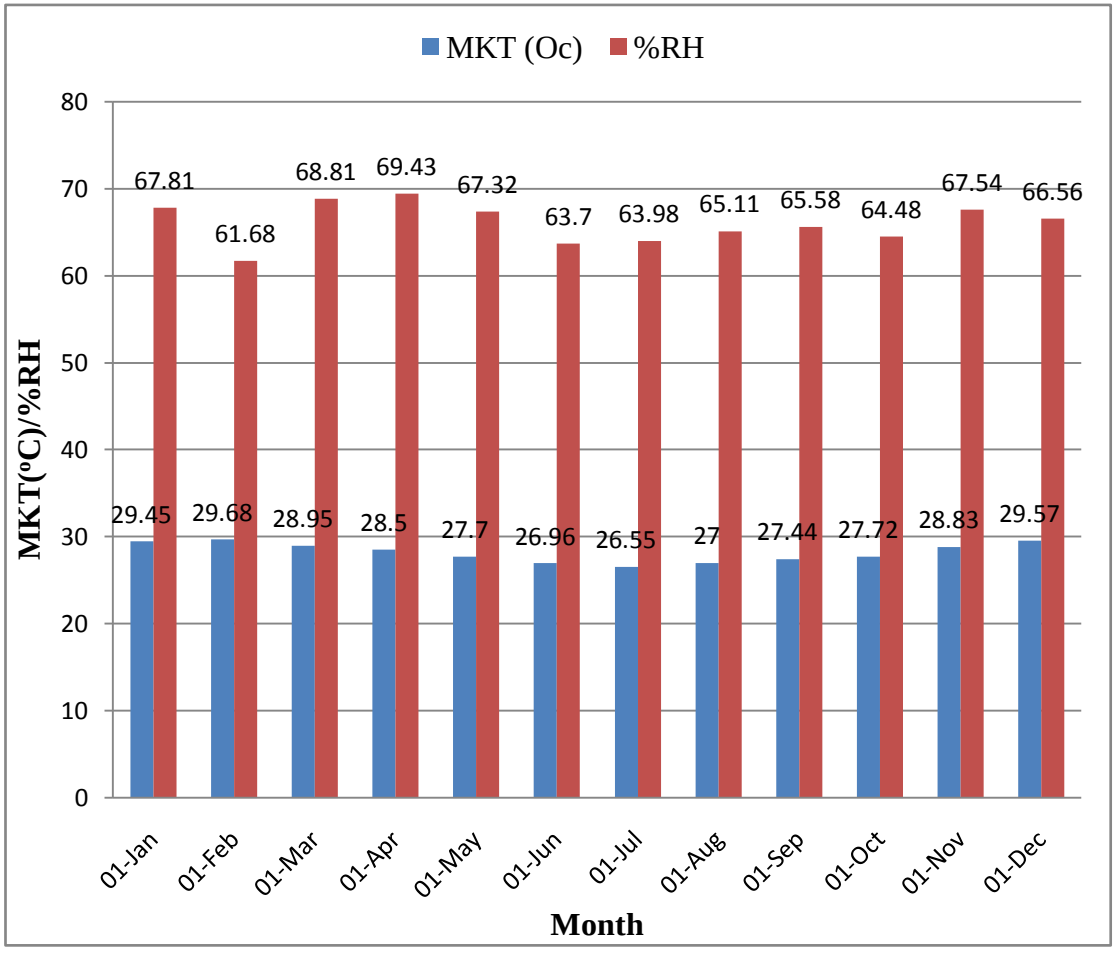

Figure 3.1.2: Trends of MKT/RH in Coastal Zone for the year 2012/2013

The Mean Kinetic Temperature in the Lake zone facilities was observed to be constant because most of them use air conditioners 24 hours. The highest temperature was found in October and the lowest in December. And thus the range in this region was 1.14 ^{o}C.

The relative humidity in this zone was found to fluctuate and being was high in December, April, November and the lowest were in July, June and August.

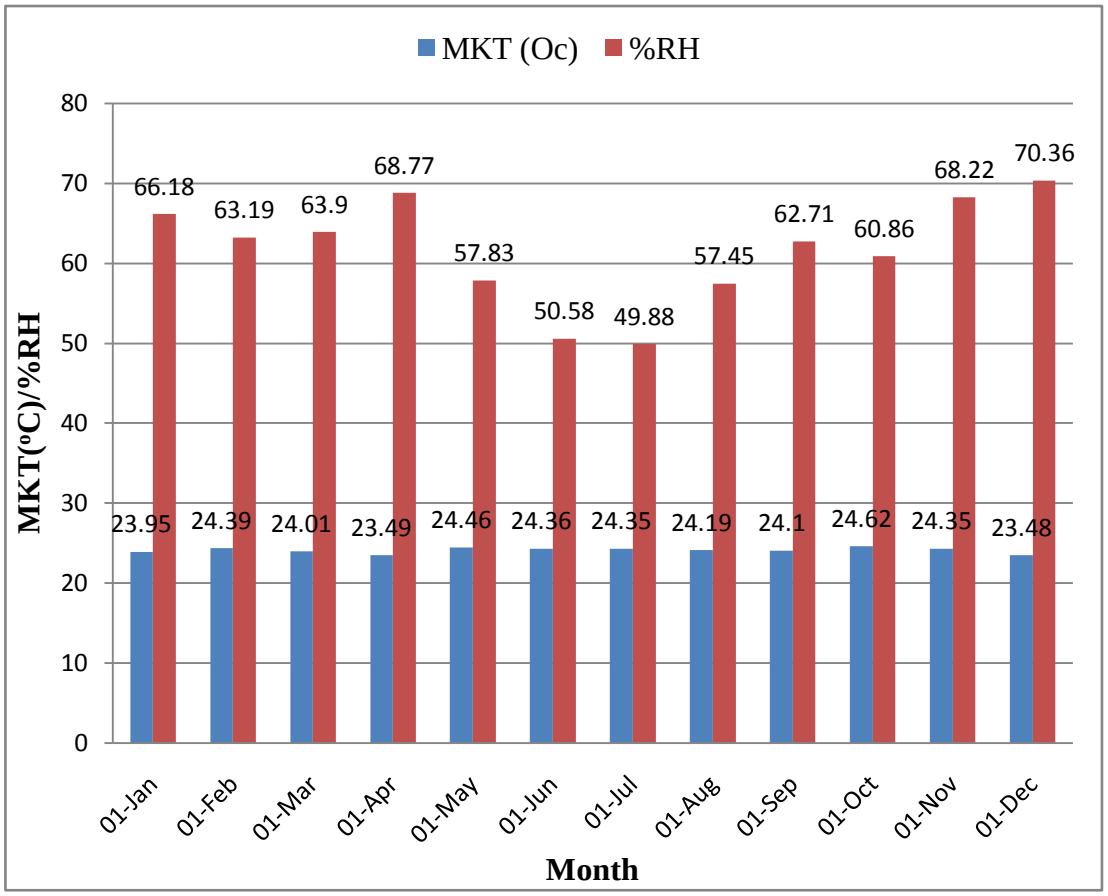

Figure 3.1.3: Trends of MKT/RH in Lake Zone for the year 2012/2013

In figure 3.1.4 below, the calculated Mean Kinetic Temperature value in Southern highland zone was low throughout the year because in that area the climate is cold. The highest temperature (MKT) was found in October and the lowest was in July.

In the bar chart below, the relative humidity was seen to increase as temperature decreases and it was high in April then started decrease up to October.

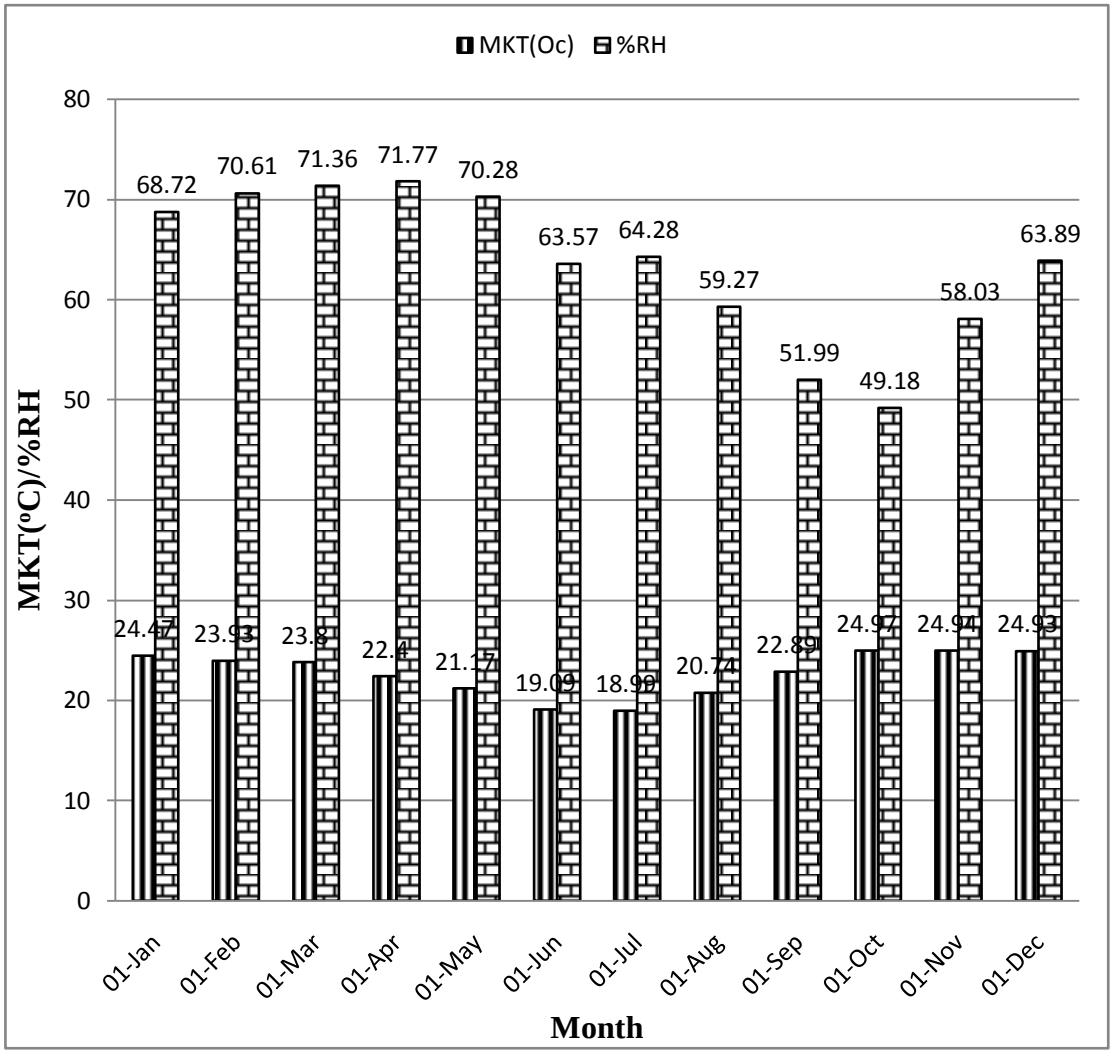

Figure 3.1.4: Trends of MKT/RH in Southern Zone for the 2012/2013

Mean Kinetic Temperature in Northern zone was found to be similar to that of Southern zone (figure 3.1.5), the highest Mean Kinetic Temperature calculated was in March and the lowest was in July.

The mean relative humidity fluctuated throughout the year, and the highest was found in May and the lowest was in February.

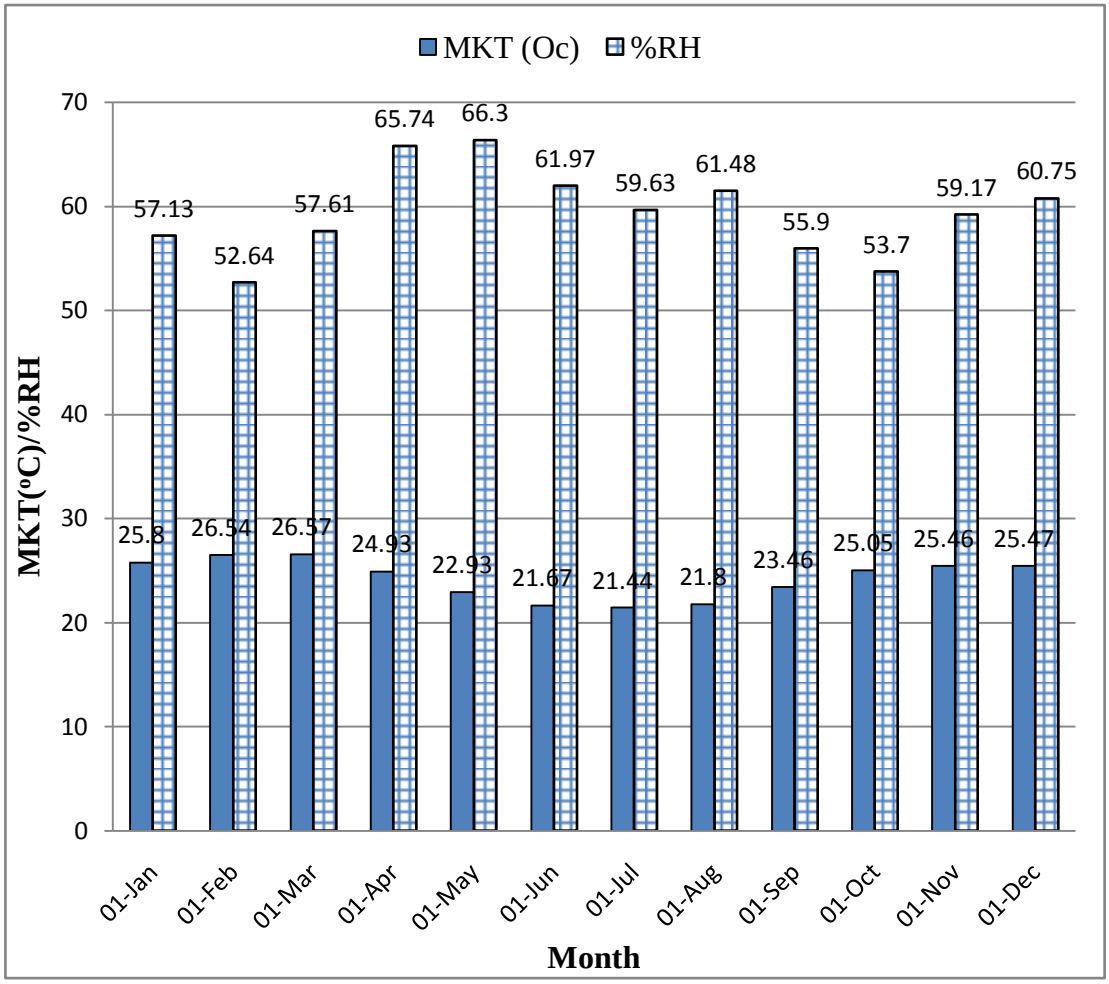

Figure 3.1.5: Trends of MKT/RH in Northern Zone for the year 2012/2013

The Western zone appeared to be dry most of the time and the temperature seemed to be high and remained constant (figure 3.1.6). The highest and lowest temperature was in September and in July respectively.

The highest relative humidity was in April while the lowest was in October. The relative humidity range in this region was found to be high because almost all facilities visited in six zones of Tanzania were not installed with humidifier/dehumidifier.

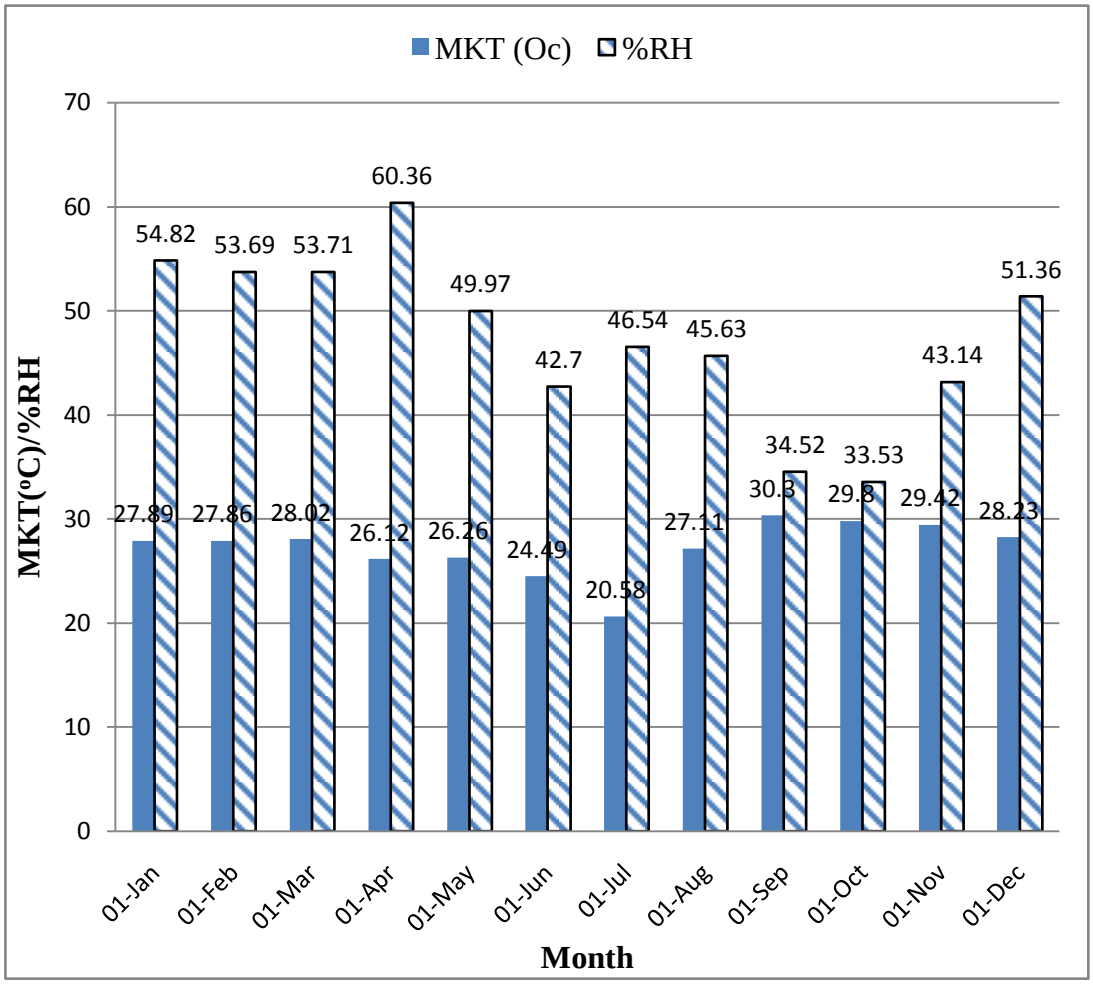

Figure 3.1.6: Trends of MKT/RH in Western Zone for the year 2012/2013.

3.1.3 Mean Kinetic Temperature variation with period time

The temperature data fluctuations led to variation in the Mean Kinetic Temperature in different months (figure 3.1.7). Thus, the temperature was high in January, February, March, April, October, November and December but in May, June, July, August and September was low. The highest Mean Kinetic Temperature calculated was in February, and gradually decreased to its lowest level in July then increased to December.

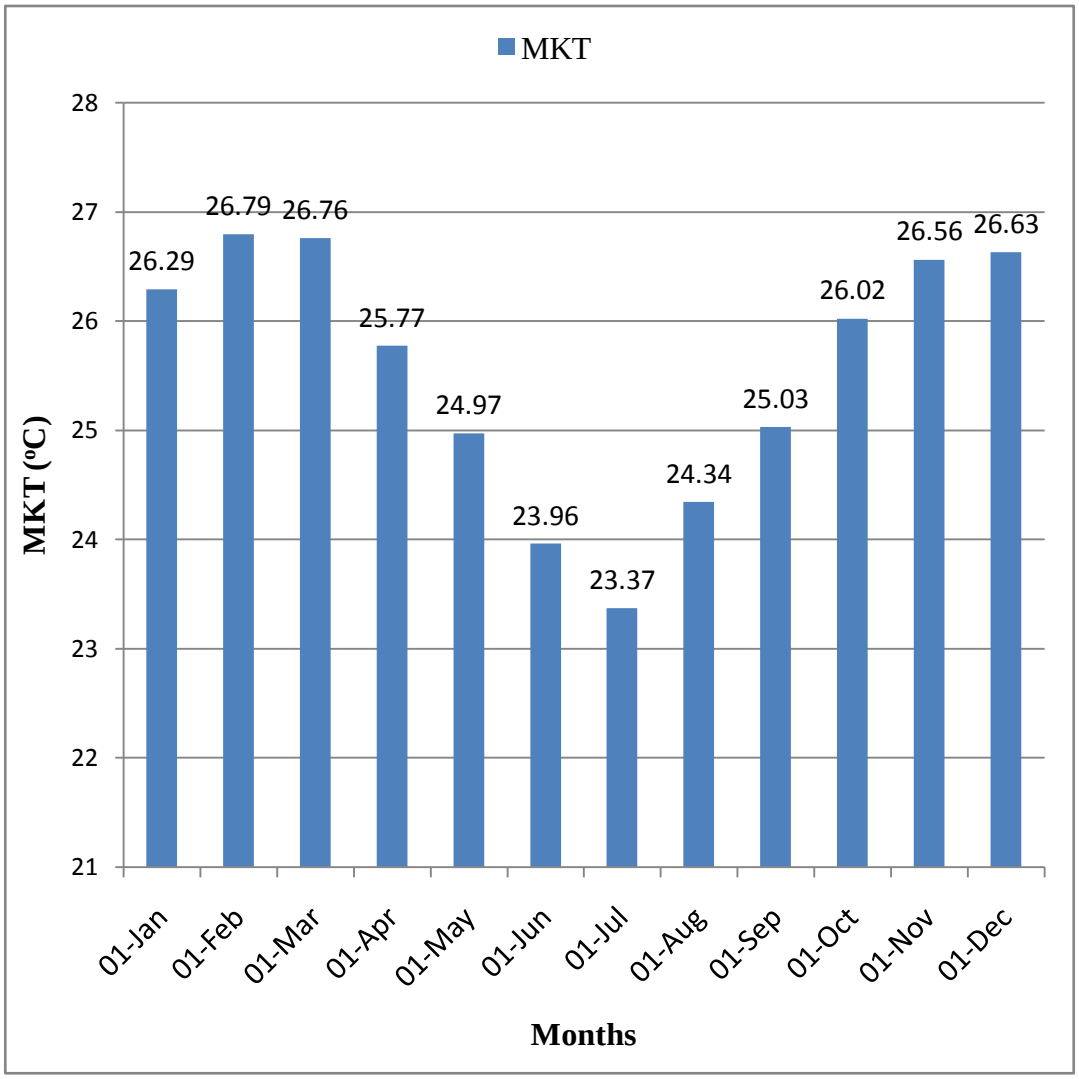

Figure 3.1.7: The Mean Kinetic Temperature in a year (Aug 12-Jul 13) for each month

Figure 3.1.8 shows that the highest arithmetic mean for relative humidity was in April, March and December in a year. However, the relative humidity in October, September and July were 54.05%, 55.73% and 57.15% respectively, and were found to have low arithmetic mean compared to the rest of months in a year.

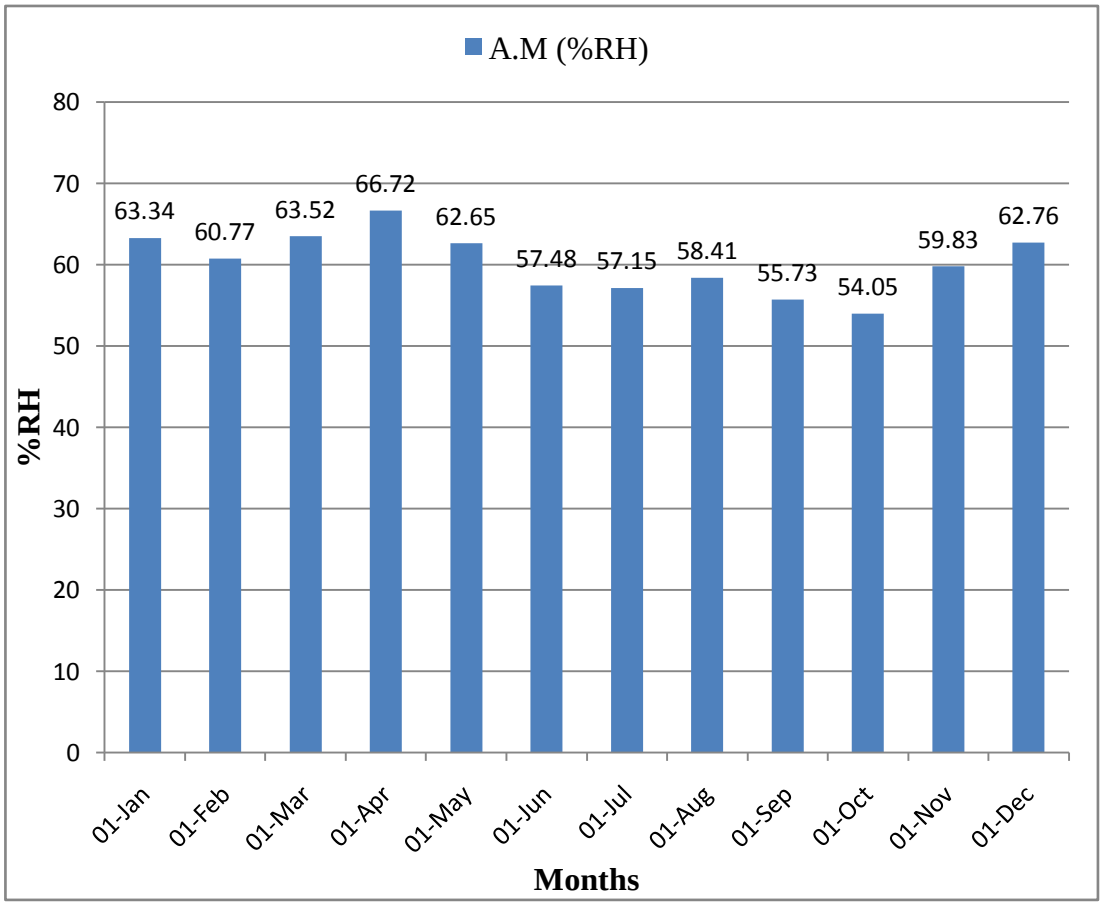

Figure 3.1.8: The Relative Humidity in a year (Aug 12-Jul 13) for each month.

The trend of temperature (MKT) in the facilities selected in each of six zones is shown in figure 3.1.9. The temperature in the central zone facilities was observed to be relatively constant when compared with other zones. Temperature in the coastal zone facilities was high in comparison with other zones, this was because most warehouses and pharmacies were installed with AC's but sometime the same were switched off for the purpose of expenditure and also in the coastal zone the temperature was high due to the sea around.

In the Lake zone, generally the temperature was not much high for reason that about 50% of the facilities visited were using air conditioners. For the Southern highland zones the climate of that region was cool almost for the whole year. The temperature in the Northern zone was low almost the same with Southern zone though somehow higher. Western zone temperature was much more fluctuating and sometimes they

did/did not use AC's. That region is dry almost over a year so it contributed to the temperature to be high.

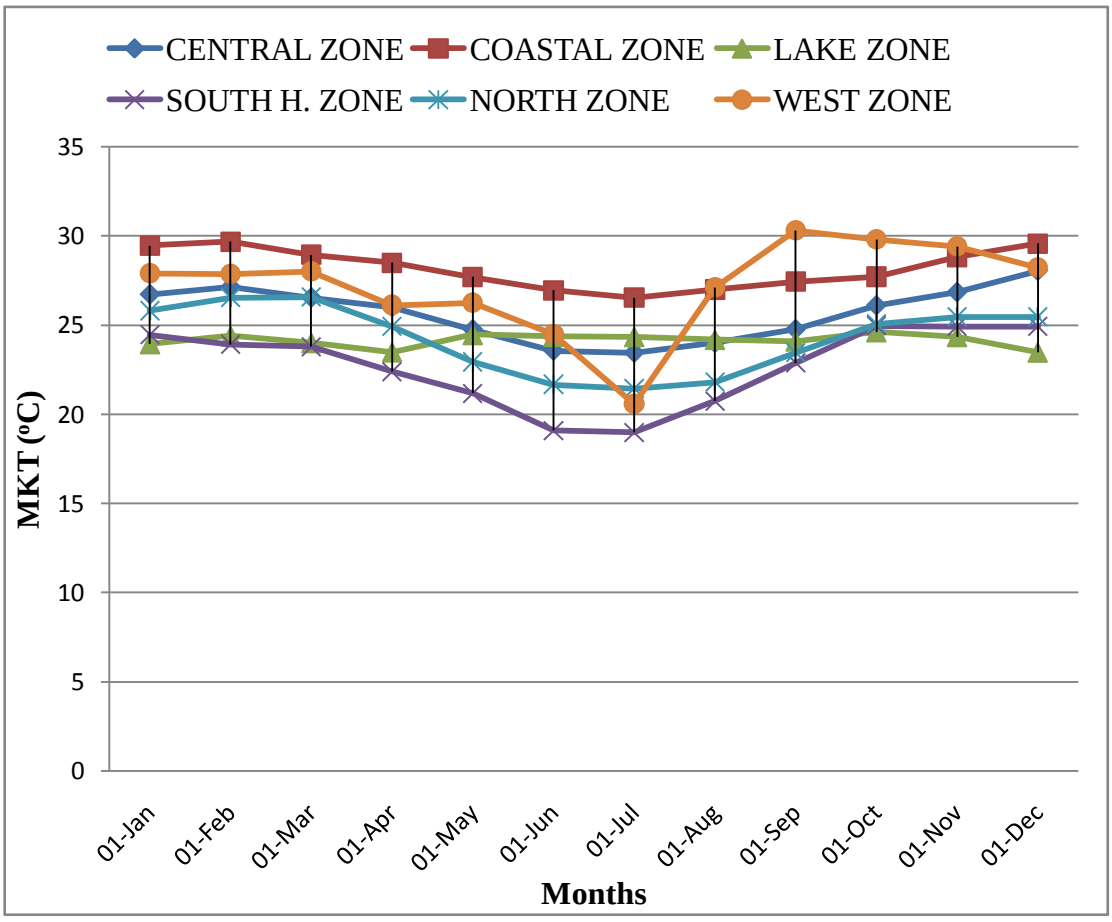

Figure 3.1.9: The Mean Kinetic Temperature in six zones versus months in the year 2012/2013.

The relative humidity in all six zones was fluctuating except for the coastal zone, where most months were observed to have much higher relative humidity (figure 3.1.10). However, in the Western zone the relative humidity was observed to be low in most of the year and was found to be much lower in September and October.

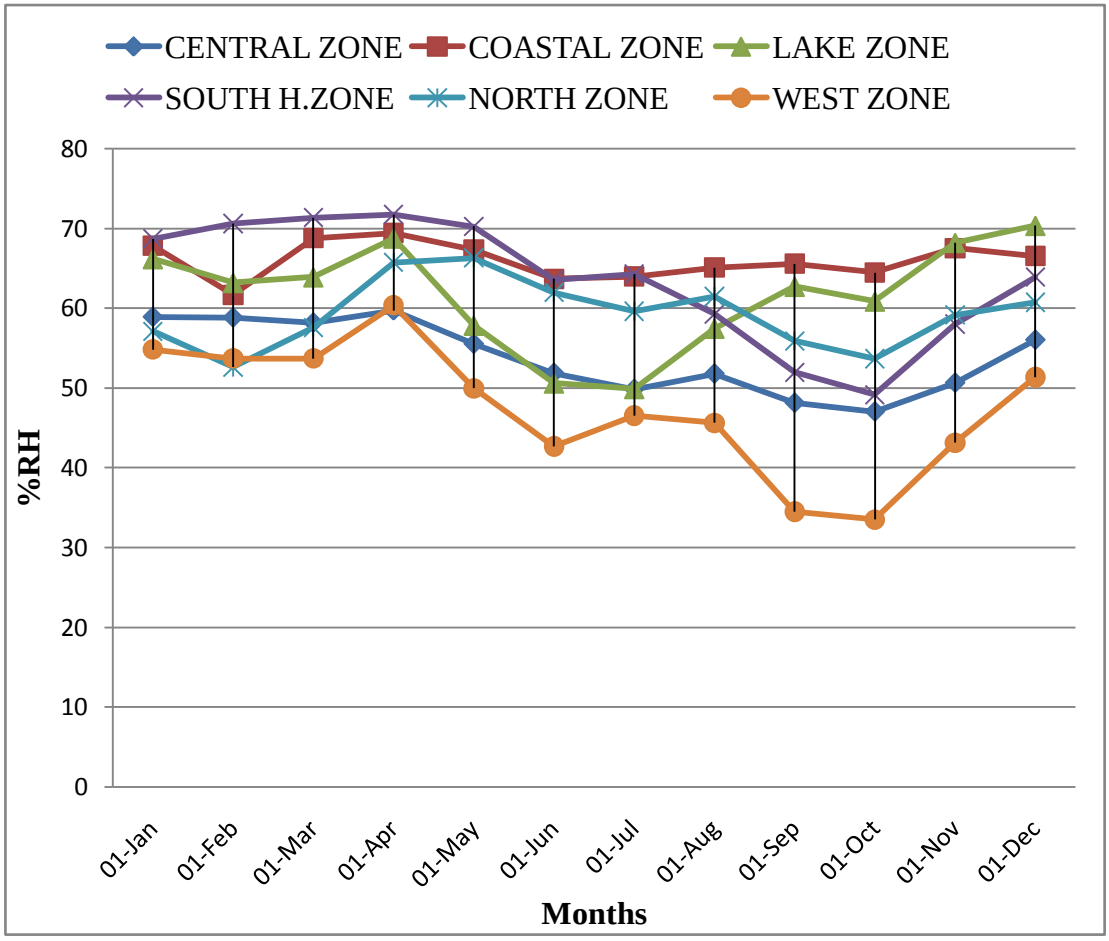

Figure 3.1.10: The Relative Humidity in six zones versus months in the year 2012/2013

3.2 DISCUSSION

The pharmaceutical manufacturers determine drugs shelf life or expiration date by using stability testing [27]. Stability testing ensures that drug's potency and integrity are intact over a specific period of time. A drug can lose its potency before the expiration date when exposed to oxygen, light, humidity or high temperature [28].

Molecules move more rapidly at higher temperatures, so heat accelerates the chemical reactions that cause deterioration. The amount of water vapor in the air is important for two reasons: moisture provides fuel for the chemical reactions that cause deterioration, and it causes physical damage such as swelling and shrinking. Thus, higher relative humidity results in a quicker deterioration rate. Very low relative humidity can result in desiccation and cracking of some materials [29].

The coastal zone has been observed to maintain high (warm) temperature from October to April but it falls from May to September. Thus, from this observation, most facilities did not use air conditioners though they are installed. Some of the facilities windows and doors were always open, hence providing enough cool air circulation. However, the Southern highland zone showed that from November to May the relative humidity was high compared with that of June to October which suggests that most areas of Southern Tanzania had more rain during that time of the year, as a result it creates high vapor (humidity) in the environment and may affect the controlled storage conditions if facilities found open. It was found that 100% of the facilities surveyed were not installed with humidifier/dehumidifier.

The analysis conducted showed the mean kinetic temperature was 25.63 ^{o}C and at the same time, the mean arithmetic relative humidity in all six zones was 60.2%. This implies that the current storage conditions of 30^{o}C/75% being used in stability testing for the pharmaceutical products are very high. The existence of a high variation in climate among different zones in Tanzania is a challenge in using a single storage condition.

CHAPTER FOUR

4.0 CONCLUSION AND RECOMMENDATION

4.1 CONCLUSION

Tanzania which covers a large area displays a variation in climate in different zones. For example, in Northern zone and Southern highland zone the temperature is much lower compared to the Coastal zone. The storage facilities in Tanzania do comply with the Good Storage Practice of medicines according to the International Committee on Harmonization (ICH) with respect to temperature and relative humidity. The data suggest Tanzania fits well in climatic zone IVb 30 °C ± 2 °C/75% RH ± 5% RH and Zone II (25 ± 2^{o}C/60 ±5%) according to ICH guidelines. In principle this argument holds only if the facility is fitted with air-conditioning. However, with the current requirement one puts low risk by considering the worst case scenario while on the other hand it would mean some good quality medicine are wasted as a consequence of underestimated shelf life. The economic loss resulting from this remains undetermined.

The increasing attention now is being given to the possible effects of storage and transport on the stability of pharmaceutical product. It is hoped that, this will improve confidence in community about the quality of drug products that are supplied to patients [29].

4.2 RECOMMENDATION

The study recommends mapping of storage conditions from facilities which are not fitted with air-condition in order to see whether they will also comply with ICH conditions.

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