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DETERMINATION OF MEAN KINETIC TEMPERATURE FOR SUDAN

Dr. Abdrhman Mahmoud Gamil*

Associate Professor of Pharmaceutics, Al-Neelain University, Sudan.

***Corresponding Author: Dr. Abdrhman Mahmoud Gamil**

Associate Professor of Pharmaceutics, Al-Neelain University, Sudan.

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ABSTRACT

According to Arrhenius theory, the arithmetic mean of the temperature excursions does not reflect the true degradation that takes place when a pharmaceutical product being kept at this temperature all over the storage period. The Mean Kinetic Temperature Equation given by JD Hayenes was internationally adopted to calculate this temperature. WHO classified Sudan as zone IVA depending on the meteorological data which had been taken from the shade in the open air where drugs were not stored in. The USP and FDA consider the storage facility MKT where the drugs were not transported in. The difference was found to be 3.8 °C. Transportation of medicines from Khartoum to the other states was by trucks, Lorries and plane in uncontrolled conditions. Medicines are also stored in facilities in uncertain conditions. Dataloggers were placed inside medicines cartons and transported in the usual way to five cities representing the Sudan climate and stored for 52 weeks. The recorded temperatures and humidity were then computed by the Stability System II Scienteck and hence introduced to SPSS program to compare between the stations. WHO stated that, if more than one zone exists in one country, the worst conditions should be considered. Thus, they were obtained using the dataloggers record, the meteorological records (1920- 1992) and the meteorological records for the same period of the study. Considerable excursions were recorded; the transportation temperature is highly exceeded the EMRO guidelines. It had been recommended that, the DRA should adopt dataloggers records as a means to follow up the storage conditions for licensing a medicine storage facility and to set a firm regulation for the transportation of medicines across the country. Dataloggers reflect the true conditions for transportation and storage conditions and thus it is recommended to be applied globally.

KEYWORDS: Mean Kinetic Temperature, storage conditions of medicines, transportation of medicines, climatic zoning of Sudan, Use of Dataloggers.

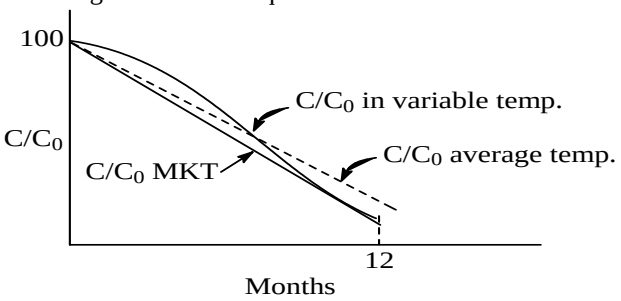
INTRODUCTION

Concept of Mean Kinetic Temperature

Mean kinetic temperature, MKT, is defined as the single calculated temperature at which the total amount of degradation over a particular period is equal to the sum of individual degradation that would occur at various temperatures (USP ,2007- 2016) It is the temperature at which isothermal storage at MKT would have caused the same drop in potency (Carstensen J, 2000). The mean kinetic temperature is a single derived temperature that, if maintained over a defined period of time, affords the same thermal challenge to a drug substance or drug product as would be experienced over a range of both higher and lower temperature and takes into account the Arrhenius equation. When establishing the mean kinetic temperature for a defined period, J.D Haynes equation could be used (ICH QAIR2).

If the temperature fluctuates between 20 and 35 °C during the year as it is generally observed during winter and summer, the average or the arithmetic mean is 27.5. The following graph will be obtained on plotting the concentration over the initial concentration against months. So that, at the end of the year, the total degradation as a result of various fluctuating temperatures equal to the degradation due to one isothermal temperature if it was maintained all over the year.

The temperature dependency is not linear but logarithmic according to Arrhenius equation.



The USP mean kinetic temperature given by Haynes

$$MKT = \frac{\frac{\Delta H}{R}}{-\ln\left(\frac{e^{-\Delta H / RT_1} + e^{-\Delta H / RT_2} + \ldots\ldots\ldots + e^{-\Delta H / RT_n}}{n}\right)}$$

ΔH is the heat of activation = 83.144 KJ.mol^{-1}, (unless accurate information available)
R is the gas constant = 8.3144x10^{-3} KJ.mol^{-1}.degree^{-1} ,T is the temperature in Kelvin, n is the number of entries, minimum of 52 week entries.

The identity, strength, quality, purity of the products should not be affected (Willig S, 2005). The FDA states that any time the yearly MKT of a facility approaches 25 °C, the occurrence should be documented, the cause should be investigated and corrective actions should be taken to ensure that the facility is maintained within the established conditions for drug product storage. FDA recognizes that when the MKT exceed 25 °C, it may not have an impact on product being stored less than one year at a time, but warning that the facility itself may not be under adequate control. However, depending on the duration and extent of such excursions and the dosage form, it may be necessary to determine if the product quality has been adversely affected (FDA, 1998).

Section 501 @(2)(B) of the Federal Food, Drug and Cosmetic Act states that a drug shall be deemed to be adulterated if the facilities or control used for holding drugs do not conform to GMP.

Methods of calculation of MKT

The USP advised to enter the frequent records for pharmaceuticals in the doctor's cars, sales representatives and patient's cars, etc. If the temperature is electronically recorded at many times during a day and all the values are used in the calculation of MKT, then there is no difference between the USP and FDA method. The USP method of calculation of the MKT gives lower values than the FDA method because of the use of an arithmetic average that is incorrect for an Arrhenius-type equation (.Kommonobiona B and Rhodes, 1999). The FDA method is therefore referred. The energy of activation 83 KJ mol^{-1} had been adopted by ICH, FDA, USP and WHO (Kommanaboyina B. and Rhodes,1999). USP method of calculation uses 52 entries, the mean highest and lowest temperature for every week for 52 weeks.

FDA method of calculation recommends that, all data obtained to be inserted directly into MKT equation. A minimum weekly highest and lowest temperature is recommended. The yearly MKT can be obtained by inserting 104 entries in the equation. Mobile Electronic time-temperature history recorders (Dataloggers) is a more capable device records the temperature at very short intervals and is able to download the temperature and humidity history record to personal computer. (USP 8/2007). A Software to compute the MKT is available commercially e.g.: http://www.stabilitysystem.com. Software assumes activation energy of 83.14472 KJ/mol.

Sudan Location and climatic profile

Sudan is bounded by latitude 10-23°N and longitude 22°-37°E. It is surrounded by the Ethiopian plateaus at the east to the eastern south and the equatorial forest belt at the south to the western south, the Red Sea at the east and the Western Desert at the west to the north. The northern part is hot and dry to the poor savannah to rich savannah to the Equatorial climate at the southern part and the characteristic Red Sea climate. Sudan is a tropical country with a mean annual temperature varying between 26 °C and 32 °C (Sudan metrological Authority Report, 2007). The hottest area lies with the northern parts. The historical highest temperature being reported is 49.1 °C in June 1978 at Dongolla at latitude 18°N. Hottest and coldest months vary according to the latitude.

The climate of the Red Sea region was greatly influenced by the red sea, providing a humid climate. The rain fall is influenced by the behavior and the nature of the inter-tropical convergence zone (ITCZ) which itself is controlled by the atmospheric pressure over the African continent. The ITCZ is the zone that separates the dry northerly wind from the south moist wind. It oscillates north and south following apparent movement of the sun. South to this zone is humid with occasional rainfall.

International records on Sudan climate

The oldest stability testing guidelines for the Arab countries (Pre-WHO guidelines) define the conditions for Sudan for the long-term stability testing as 35-40 °C. (Kopp-Kubel S and l Zahn, 1998). WHO defined Sudan as Zone III (WHO,1996) before being changed to IVa. The Sudanese governmental laboratory and the regulatory authority use these guidelines using the conditions for long-term stability testing as 30°C/45%RH. The climate of Sudan provided by the world metrological organization WMO, Geneva presented Khartoum weather as follows: (Table 2)

Month	Mean temperature		Month	Mean temperature	
	Min.	Max.		Min.	Max.
Jan.	15.6	30-8	July	25.9	38.4
Feb.	17	33	Aug.	25.3	37.3
March	20.5	36.8	Sept.	26	39.1
April	23.6	40.1	Oct.	25.5	39.3
May	27.1	41.9	Nov.	21	35.2
June	27.3	41.3	Dec.	17.1	31.8

(www.worldweather.or/085/coo249)

It has been reported as the hottest city in the world having the highest MKT 32.5°C, then Aswan 30°C and New Delhi 27.9°C.

EMRO Resolution

Table 4: WHO- East Mediterranean Office (WHO-EMRO,2006).

Testing conditions where the stability of product has been shown	Recommended labeling statement
Climatic zone III and IVA: long term 30c°/ 65% RH accelerated 40c°/75%RH	Store below 30c°
Climatic zone III and IVA: long term 30c°/ 65% RH	Store and transport below 30c°

In this way two zones exists in Sudan, Zone III and zone IVA. The recommended long term testing condition is 30c°/65%RH. With a note that the aqueous – based solutions in semi-permeable packaging, and dosage form sensitive to low humidity. (WHO –EMRO, 2006).

National Meteorological Mean Higher and Lower Temperature for the Selected Stations for 30 Years Records

Table 5.

Month	Khartoum $15^0/33'$			Portsudan $19^0/37'$			Al-Damazin $11^0/46'$			Dongola$10^0/19'$		Al-Fashir$13^0/27'$	
	higher ^{0}C	Lower ^{0}C	RH %	Higher ^{0}C	Lower ^{0}C	RH %	Higher ^{0}C	Lower ^{0}C	RH %	Higher ^{0}C	Lower ^{0}C	Higher ^{0}C	Lower ^{0}C
Jan	30.7	15.6	26	26.6	19.4	65	35.2	16.6	30	26.5	8.7	29.4	9.9
Feb	32	16.8	21	26.9	18.7	65	36.9	18.3	23	29.3	10.1	31.8	11.9
March	36.5	20.3	16	28.5	19.5	63	39.5	21.7	20	33.7	14	35.2	15.9
April	40.4	24.1	15	31.8	21.7	59	40.6	24.2	25	38.9	18.9	37.9	19
May	41.9	27.3	20	35.4	24.2	53	38.5	24.8	44	42.2	23.2	38.9	22.1
June	41.3	27.6	26	38.4	36.3	44	35.3	22.6	61	43.1	24.9	38.5	23.3
July	38.5	26.2	42	40.7	28.5	44	32.1	21.4	74	42.6	25.5	35.8	22.9
Aug	37.6	25.6	48	40.4	29	46	31.3	21	79	42.2	25.7	34.6	22.3
Sept	38.7	26.3	41	37.9	27.1	35	32.5	20.9	76	41.8	25.4	35.8	21.8
Oct	39.3	25.9	29	33.8	25.3	67	34.9	21.3	67	39	21.8	36	19.5
Nov	35.3	21	26	30.9	23.7	69	36.8	19	40	32.1	14.9	32.7	13.7
Dec	31.7	17	29	28.3	21.1	68	35.6	16.9	33	28.2	10.3	29.8	10.5

Transportation across Sudan: Medicines are stored in Khartoum at the distributor's warehouses and then distributed to all parts of the country. They are transported via passenger buses, trucks and Lorries, being exposed to the blazzy sun, open air, dust and rains. Transportation took many days to some cities from Khartoum and Medicines were suspected to be exposed to temperature exceeding 30 °C and up to 45 °C in summer.

Objectives

The main objective of the study is to determine the MKT of Sudan in an appropriate scientific way and to investigate the compliance of the real storage condition with that of the international recorded ones, comparing the MKT and relative humidity.

Methodology and Study design

The stations were selected to represent different climatic conditions in Sudan.

1. Al-Damazin: It is the main city of the Eastern South of the country where the climate is influenced by the Ethiopian Plateau. It lies at 11^0 N latitude.

2. AL-Fashir: It is the main city in Darfour state representing the Western region. It lies at 14^0 N latitude. The climate of which is greatly influenced by the western desert.

3. Khartoum: It is the central station at the middle of the country. It lies at 16^0 N lattitute. It represents the central region.

4. Dungola: It represents the Northern region. It lies at 18^0 N latitude.

5. Port sudan: It represents the Red Sea region of which climate is greatly influenced by the Red Sea. It lies at 21^0 N latitude.

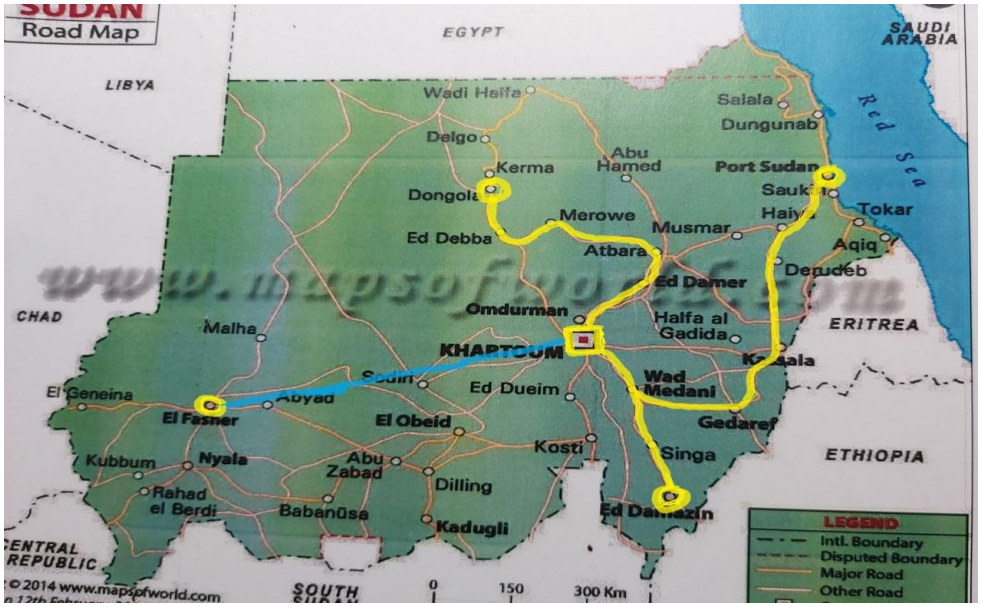


Figure 1: Sudan Map.

Dataloggers had been programmed to log data every 90 minutes, up- to more than 5000 points in 52 weeks. The readings had been barred by adjusting the screen not to display the recorded data.

Temperature and humidity data logging devices

Five electronic devices are used, from SATO KEIRYOKI MFG. CO. LTD. TOKYO 101 – 0037 JAPAN SK- L 200II series data loggers No. 8171–00 model SK–L 200THII. With Probes sensitive for temperature of thermistor type which is recommended by USP and a high polymeric resistance change humidity sensor. Software SK– L 200 / L 200 II series software, SK Sato Data logger for windows, version 5.11 E.

Treatment of Data

Data had been downloaded in *hp* computer. Then it had been transferred to CVS spread sheet and to note pad program. Then the MKT had been calculated using USP and FDA methods. The software used was Scien Teck stability system II software for calculating MKT by Dr.Yang using and activation energy 83.114 KJ Moe -1. Then results of both methods are compared to the international MKT of Sudan. The MKT was computed for each station using the datalogger data, meteorological data, and data of WMO. The monthly mean of the minimum and maximum temperature and the monthly average RH % for the years 1962 to 1991 were used, then the results had been compared using SPSS statistical program. Then concluding the worst condition MKT and thus locating the country in the international zoning system.

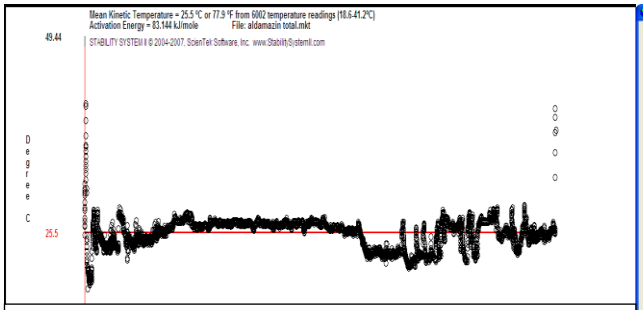
RESULTS

Table 6: The Mean Kinetic Temperature and the Relative Humidity of transportation.

Station	Vehicle	Transportation conditions	
		MKT °C	% RH
Damazin	Truck	33.1	15.7
Dongola	Passenger's bus	34	16.6
Fashir	Airfreight	30.6	15.8
Portsudan	Distribution truck	35.9	18.9
	Passenger's bus	45.2	26.3
Khatoum	Private car	48.3	13

Table 7: The MKT and the average RH for the storage facilities at each station.

Station	Adopted meteorological data		Meteorological data in the period of the study		Study data of dataloggers	
	MKT	RH	MKT	RH	MKT	RH
Al-Damazin	28.5 ^{0}C	47.7 %	31.7 ^{0}C	50.4%	25.4 ^{0}C	41.3%
Dungola	29.4 ^{0}C	N. A	33.8 ^{0}C	23.1%	27.2 ^{0}C	22.9%
Al-Fashir	26.9 ^{0}C	N.A	27.8 ^{0}C	19.4%	28.8 ^{0}C	19.4%
Khartoum	30.8 ^{0}C	28 %	31.6 ^{0}C	37.8%	27 ^{0}C	28.2%
Port-Sudan	29.4 ^{0}C	58.2 %	39.1 ^{0}C	39.1%	25.6 ^{0}C	52.2%



Al-Damazin MKT Computed from datalogger Records

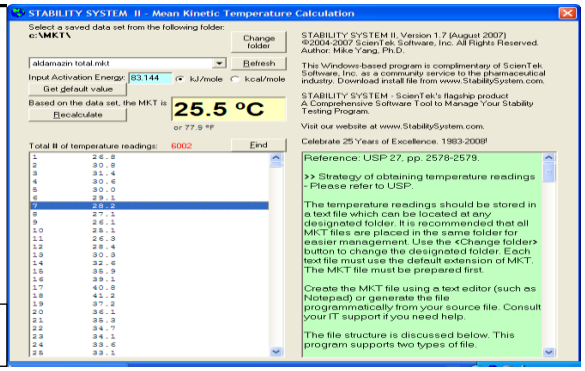
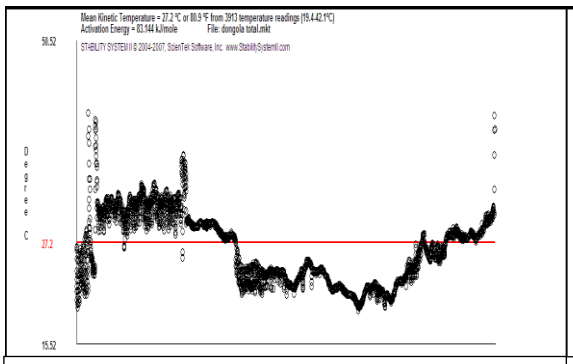
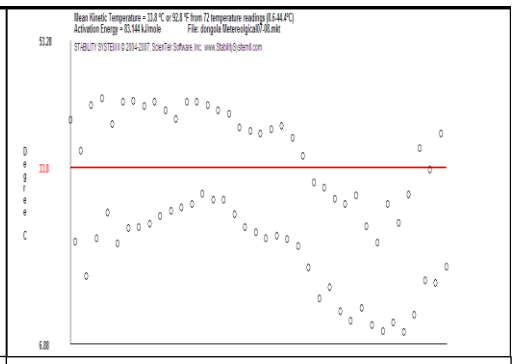


Figure 2: Al- Damazin Records.

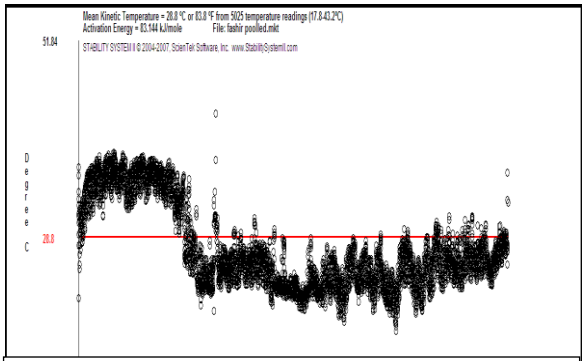


Dongola MKT computed from Datalogger Records

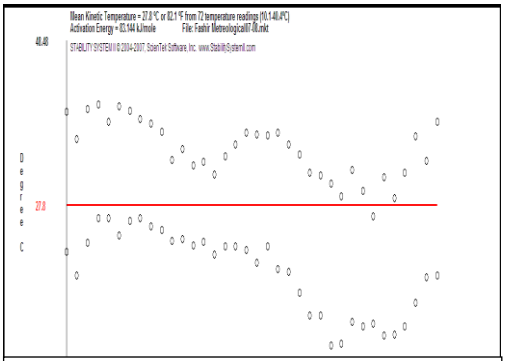


Dongola MKT computed from Meteorological Record

Figure 3: Dungola Records.



Al-Fashir MKT computed from datalogger records



Al-Fashir MKT computed from Meteorological Record

Figure 4: Al- Fashir Records.

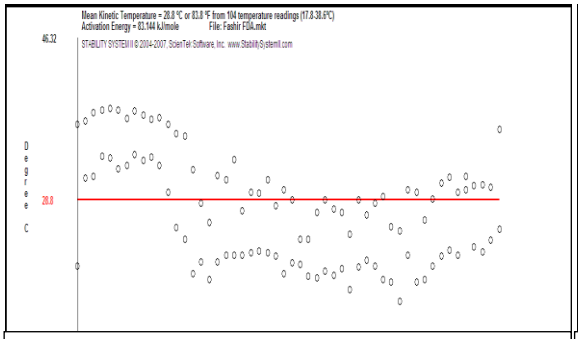


Figure 5: Al-Fashir MKT computed according to FDA method.

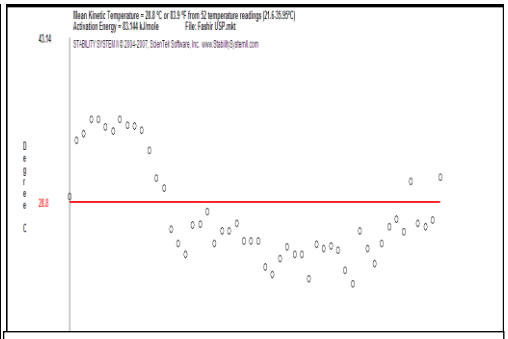


Figure 6: Al-Fashir MKT computed according.

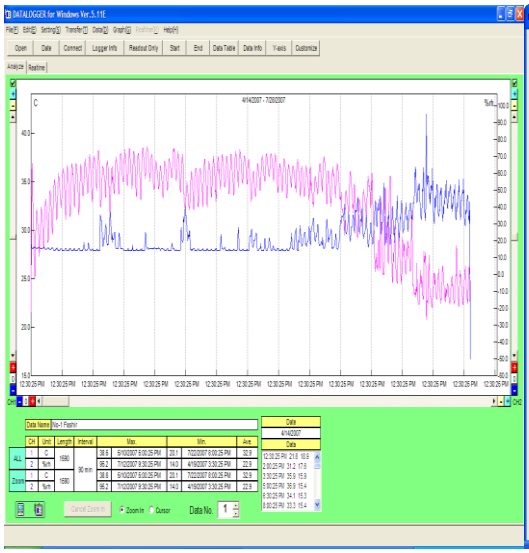


Figure 7: Results from the Datalgger.

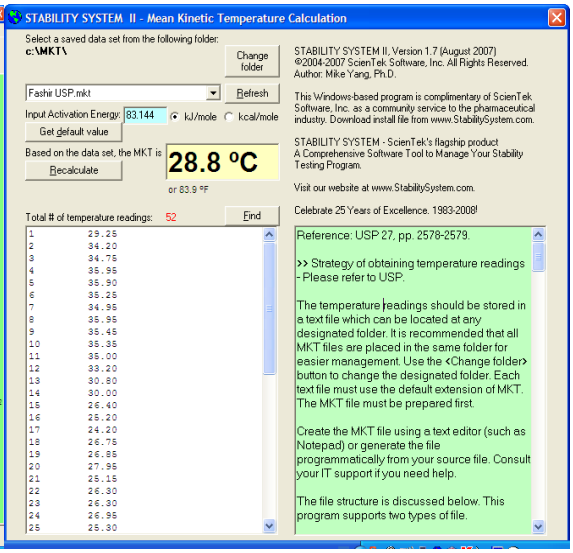


Figure 8: Computation of Results.

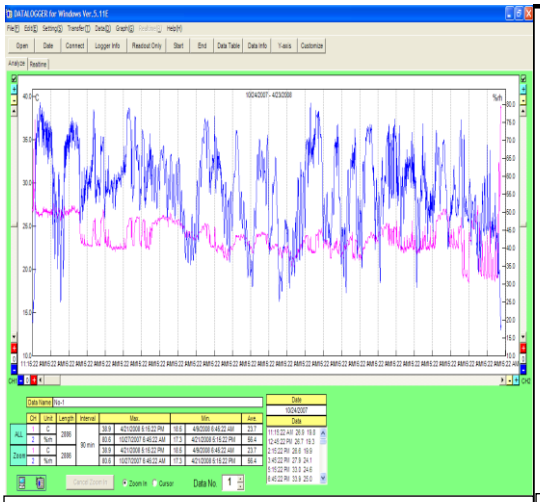


Figure 9: Portsudan Results from datalogger records.

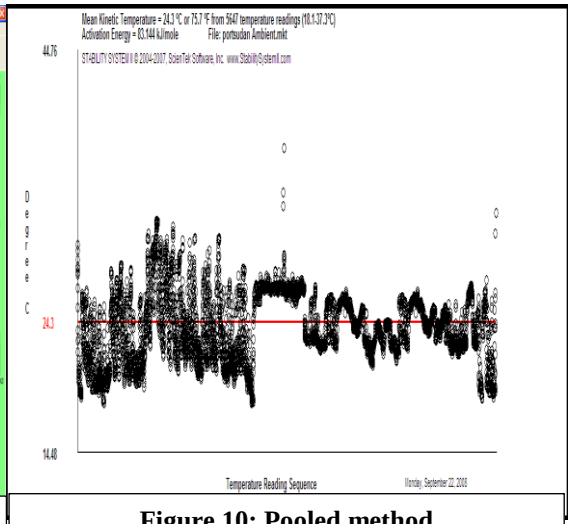


Figure 10: Pooled method

Khartoum MKT Results

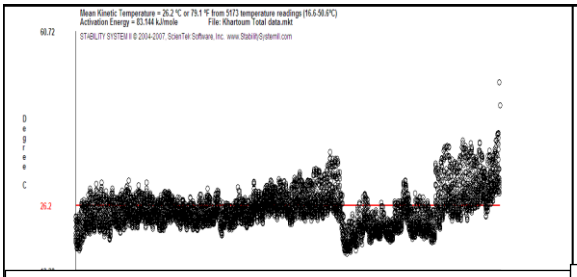


Figure 11: Khartoum Station- Datalogger Records.

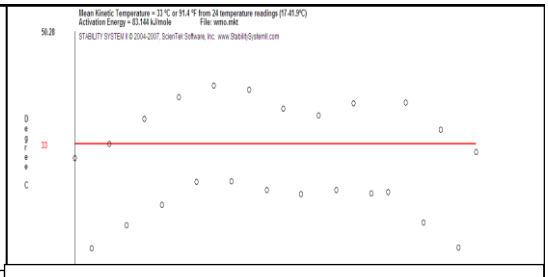


Figure 12: Khartoum MKT calculated from WMO Records.

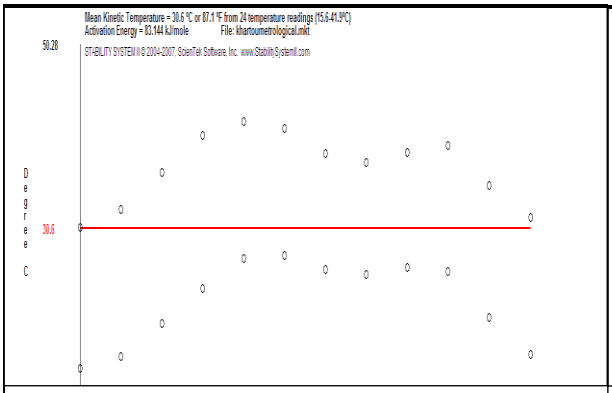


Figure 13: Khartoum MKT calculated from Meteorological Records (1962 – 1991).

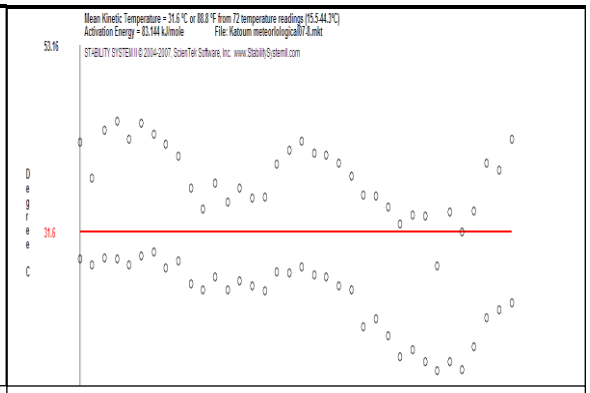


Figure 14: Khartoum MKT calculated from Meteorological Records (4/2007 – 3/2008).

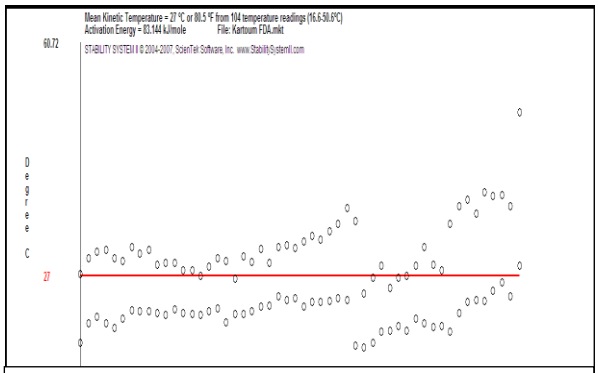


Figure 15: Khartoum MKT calculated by USP Method.

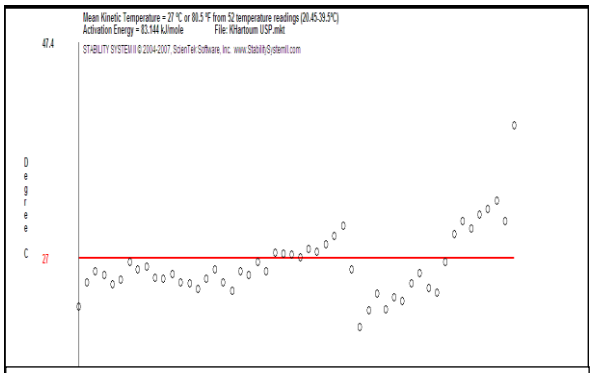
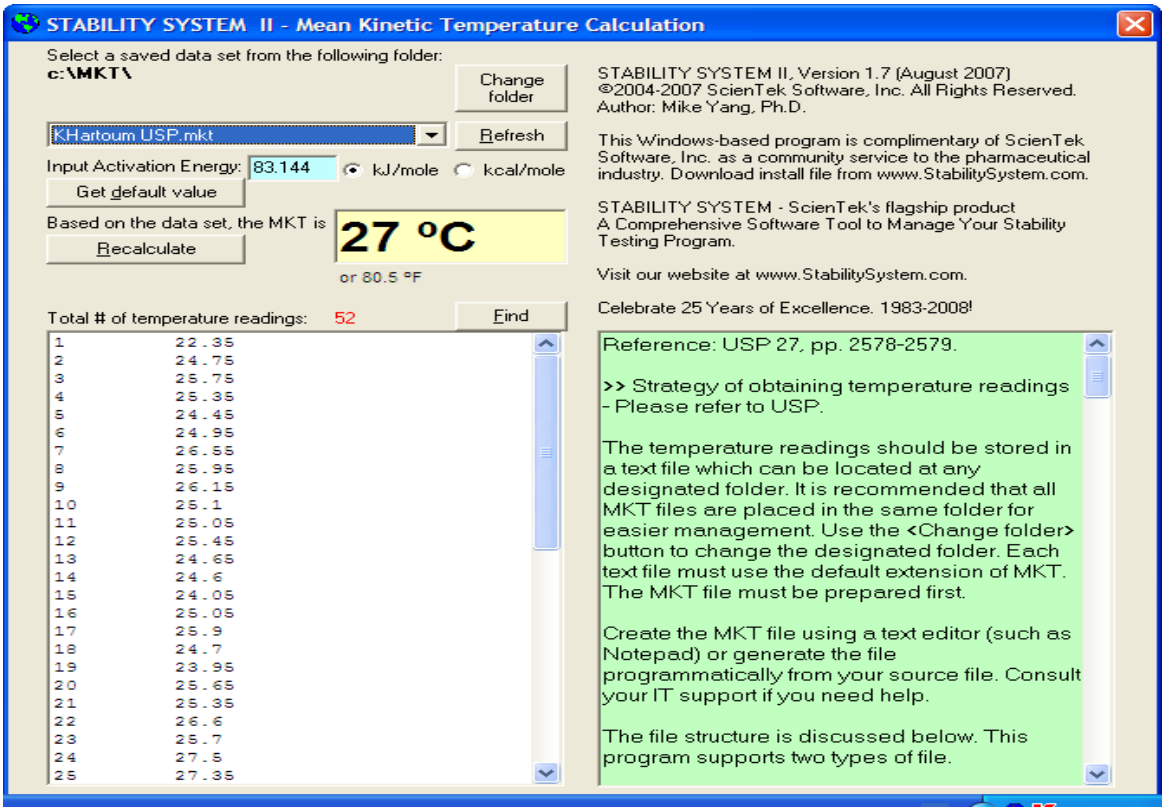


Figure 16: Khartoum MKT calculated by FDA Method.



DISCUSSION

Transportation Temperature

Table (6), it is clear that the transportation MKT for the five stations was above 30°C contradicting the EMRO stability guidelines instructions which states that the transportation conditions for Sudan should be < 30°C. The results obtained were significantly different from 30°C with a significance value 0.033 and t-value 2.757. Transportation conditions via the usual routes and vehicles varies from 48.3°C which is the MKT of a private car in Khartoum to 30.6°C; the plane temperature to Al-Fashir. This result was in conformance with the result of the IDA field study which indicated that the temperature at the port may reaches up to 45°C (Hogerzil *et al*,1990). The temperature inside a private car reached up to 50°C with an average of 48.3°C; which is harmful to medicinal products and this may take place inside doctors' cars especially the medical representatives who are always taking their samples in the car back or cabinet for many days during their daily work. It may also take place inside the distribution vehicles that are not conditioned. Thus, theoretically, the conditions specified and the expiry date defined will not be real. Increase in 10 °C, from 20 to 30 °C increases the degradation 1.76 folds. If the rate constant be estimated by fitting the Arrhenius equation, it is possible to estimate the time required for 10% degradation (t_{90}) where reciprocal of t_{90} is related to temperature. (Yoshioka S, 2000).

Transportation Humidity

The five stations showed transportation humidity ranging from 13% to 26.5%; less than 35% indicating the dry conditions of transportation, in this case the EMRO stability guidelines requires special testing for liquids and aqueous preparations in permeable or semipermeable containers.

Storage conditions

The MKT and the average relative humidity of the five stations constituting the storage condition for various sources of data were presented in table (8).

Table 8: Calculated storage conditions of the five stations according to Dataloggers data.

Method	Damazin station		Dongola station		Al-Fashir station		Khartoum station		Portsudan station	
	MKT	RH%	MKT	RH%	MKT	RH%	MKT	RH%	MKT	RH%
Pooled	25.4	41.3	27.1	22.9	28.8	19.4	26.2	28.2	24.3	52.2
USP	25.6	41.3	27.2	22.9	28.8	19.4	27	28.2	25.6	52.2
FDA	25.6	41.3	27.6	22.9	28.8	19.4	27	28.2	25.6	52.2
Calculated storage conditions of the five stations according to the National records										
Records	**Damazin station**		**Dongola station**		**Al-Fashir station**		**Khartoum station**		**Portsudan station**	
	MKT	RH%	MKT	RH%	MKT	RH%	MKT	RH%	MKT	RH%
Adopted	28.5	47.7	29.4	18	26.9	18	30.6	28	29.4	52.2
parallel	31.7	50.4	33.8	23.1	27.8	26.2	31.6	37.8	30.8	39.1
International Records on storage conditions of Sudan										
JTC	**WHO (WHO, 2004)**		**EMRO**		**USP calculated**		**USP derived**		**WMO calculated**		**Grimm**	
MKT	MKT	RH%	MKT	RH%	MKT	RH%	MKT	RH%	MKT	RH%	MKT	RH%
32.5	30	35	30	65	27.1	35	30	35	33	35	32.5	35

From the above table, it could be concluded that all samples at all stations were expoesd to temperature more than 25°C % for the most period of storage with a considerable excursions over 30°C % and this was contradicted to the labeled storage instructions for most products. The FDA specifies two excursions up to 30°C % after which the storage facility will be disqualified.

MKT

There are three categories of results according to source of data: Table (8)

1- MKT calculated from dataloggers by FDA, USP and pooled methods.
2- MKT calculated from the National Meteorological records.
3- Internationally published MKT for Sudan Grimm, JTC and WMO.

The values of MKT calculated from dataloggers records, were introduced to SPSS software, one-way ANOVA analysis tool using level of significance 0.05. It appears that:

1- The in-house MKT depends mainly on the interventions to improve the storage conditions, so it differs from one facility to another. The MKT values of Damazin, Portsudan and Khartoum hospitals were insignificantly different (25.2, 27, 25.2 °C respectively.
2- The MKT of Fashir was higher because the temperature readings increases during the period from 3 PM to 11 PM and decrease during the

working hours indicating that workers tend to switch off the conditioning equipment and close the pharmacy at 3 PM.

3- On comparing the MKT calculated from the adopted national meteorological records, the records for the parallel period of the study and WHO MKT for Sudan, it could be concluded that there was insignificant difference between the three results considering that, the MKT calculated from one source was for all stations taken as one group compared with the other sources. One-way ANOVA significance were (0.074, 0.243, 0.493 Thus it could be concluded that the calculations of WHO were based on the mean meteorological data.
4- Al-Damazin, Dongola, Fashir, Khartoum: There were significant differences between MKT calculated from datalogger records and that calculated from both meteorological records and WHO defined MKT having significance 0.00. The MKT calculated from recent and past National meteorological records for Damazin were significantly different from each other and from that defined by WHO. This indicates that WHO MKT was significantly different from MKT calculated from both meteorological data for Damazin having significance 0.00.
5- Portsudan: WHO defined MKT was significantly different from MKT calculated from datalogger records and from that calculated from meteorological data 0.00, 0.031. On Comparing the MKT from WMO report, the MKT defined by JTC – Badawi (Carstensen 1995), the MKT that defined by Grimm (Grimm, 1998)with those calculated from datalogger and meteorological records, the following comments can be concluded:

- The only insignificant difference was between JTC (Carstensen 1995), Grimm and Badawi (Grimm,1998) and WMO with significance value (0.098 -0.562)
- There was insignificant difference between MKT calculated from Khartoum meteorological data and that defined by JTC and Grimm (sign. 0.748).

On Comparing the USP Calculated MKT; 27.9 °C, to the MKT calculated from dataloggers at all stations, there were insignificant differences between MKT of dataloggers for Dongola, Fashir, and Khartoum; significances 0.351, 0.161, 0.82 respectively.

Comparing MKT calculated from various sources of data

1- MKT obtained from the past meteorological data (1962-1991) was insignificantly different from that of WHO, EMRO and derived MKT of USP, but it is significantly different from the MKT calculated from the recent meteorological data and from the MKT obtained from dataloggers calculated by pooled, USP and FDA methods.
2- The MKT defined by WHO was only in conformance with the MKT calculated from the past and recent meteorological data (sig. 0.142, 0.392) indicating that this is source of data.
3- There was insignificant difference between USP calculated MKT and that calculated from dataloggers using different methods and the past meteorological data, but it was significantly different from the recent meteorological data and WHO.

The average mean of MKT of the open air is 3.8 °C above the inhouse MKT and it was contrary to the international records which pointed that the measured room temperature was 7.8, 4.1, 1.6 and 1.9 above the open air temperature for zone I, II, III, IV respectively.

Average Relative Humidity

The average relative humidity of the stations was significantly different as shown by One-way ANOVA having significance value (0.00). The multiple comparisons show the following results:

1- There was insignificant difference in the average relative humidity between Portsudan, Damazin (sig. 0.065) but there was a significant difference in the average relative humidity of these stations and the other three stations (sig.0.00).
2- There was insignificant difference in the average relative humidity between Dongola and Fashir with significance value 0.838.
3- On comparing the average RH% obtained from all sources of data to the internationally published data, all results were insignificantly different from each other except the result defined by EMRO2 which is significantly different from all results with sig. value 0.001.
4- There was insignificant difference in RH% obtained from dataloggers data, past and recent meteorological records for Damazin and Portsudan and that pointed out by EMRO with a level of significance 0.104, but they were significantly different from WHO RH% (35%) sig. 0.001.
5- The average room relative humidity was 6% and 6.4% lower than that measured in the open air as recorded by the adopted meteorological records for Portsudan and Damazin respectively.

It could be concluded that by application of this method on the Asian countries, new real results could be obtained and new storage conditions may take place.

WHO recommended that, wherever two or more climatic zones exist at one country, the storage conditions should be based on the worst conditions. So, the worst condition in sudan in table 10.

Table 10: The Worst Storage Conditions.

Source of date	Worst MKT	Station	Worst humid	Station	Worst dry	Station
1962-1991 meteorological	**30.6 °C**	Khartoum	**52.2%**	Portsudan	**18%**	Dongola
The same period meteorological	**33.8°C**	Dongola	**50.4%**	AlDamazin	**23.10%**	Dongola
Datalogger in-house	**28.8°C**	Fashir	**52.20%**	Portsudan	**19.40%**	Fashir

CONCLUSION

Transportation Conditions

Transportation conditions were the most drastic conditions faced drugs along the distribution chain of drugs. Temperature reached up to 48.3 °C at town streets and the lowest temperature was 30.6 °C. Thus, transportation MKT values across sudan, were above 30°C; the specified limit of EMRO. On comparing the transportation MKT of various cities using statistica one sample test, it was found to be significantly different, of significance 0.033 and t-value 2.757 from the EMRO limits.

MKT for Sudan

The concept of the MKT was adopted world wide. It is a single derived temperature reflecting the effects of a range of temperature floculating over agiven time. The main disadvantage of WHO calculations is that, it utilizes the meteorological data which was taken from the shade at the open air where drugs were not stored in the difference is 3.8°C. The USP and FDA recommended that storage conditions should be calculated from drugs warehouses, hospitals and pharmacies where drugs are usually stored in. The principle of encoutering the worst conditions in the countery was quite justicious, so the worst storage conditions of the five stations utilizing different sources of data was stated in table (10).

All international records on the MKT of Sudan were correctely defined it, but they did not refelect the true value for the whole countery because these records calculate the MKT from sources of data that were truly existing and differing. WHO defined MKT was based on the past adopted meteorological data (1962-1991), WHO pointed 30°C as the MKT for sudan taking the mean of MKT for the whole countery disregarding the principle of encountering the worst conditions which was Khartoum 30.6 °C and those locations having more than the MKT value as in the meterological records for for the same period of the study at Dongola (33.8°C). The MKT calculated from dataloggers, MKT from adopted and the parallel meteorological data for Khartoum, Damazin, Dongola and Fashir were significantly different from that defined by WHO. The MKT calculated using one source of data for one station was insignificantly different from the MKT obtained using the same source of data for another station. JTC and Grimm defined MKT for Sudan 32.5°C was apporoved to be in conformance with that calculated from WMO record and was found to be insignificantly different from the Khartoum conditions of metereological records for the period of the study. USP calculated MKT (27.9°C) was insignificantly different from that obtained by calculating dataloggers records for the in-house conditions except MKT of Damazin, Khartoum and Portsudan which were lower than USP calculated MKT. Although USP derived value was 30°C making 2.1°C as conservative value. The storage temperature of the five station was ranging from 25.2°C to 28°C. The highest MKT was reported for Fashir Hospital where they use to switch off the air conditioner after the working hours. The diference in means of in-house daily MKT and that of the shaded open air MKT was 3.89 °C.

All published records considered the relative humidity as 35% which represents the mean of the higher and lower humidity, but this was incorrect because it had been approved that some areas were more humid throughout the year while others were very dry. The EMRO considered the MKT value as 30°C, and made attension to the humid areas by defining zone IVa for Sudan pointing 65% as a relative humidity. EMRO guidelines cosidered the dry areas by recommending that special conditions should be considered for liquids in semipermeable containers. All records disregarded the transportation conditions except EMRO which stated that transportation MKT should not be more than 30°C.

WHO defined MKT was based on the open air readings where drugs were not stored in, while USP relied upon the in-house readings where drugs were not transported in.

The mean of stations MKT being calculated from the metereological data for the same period of the study is 3.89°C above the mean of stations MKT being calculated from dataloggers data. That was due to man intervention by using air cooling equipment at facilities were drugs were stored.

Using Dataloggers facilitated adherence to the most probably true coditions, they provided readings for the true transportation conditions in the open air, on the blazzy sun and on the back of trucks. The worst transportation MKT was 48.3°C obtained at Khartoum streets and the worst storage MKT was 28.8 obtained at Fashir.

Humidity

Average relative humidity defined by EMRO (65%) was isignificantly different from that recorded by dataloggers and meteorological records for Damazin and Portsudan. The dry conditions reported by both dataloggers and metereological records on Khartoum (35%) and the very dry conditions of Dongola and Al-Fashir (18% and 19%). The room relative humidity was 6 to 7 % lower than open air reltive humidity.

Recommendations

Drug Regulatory Affairs should have to take regultory quick actions concerning drug transportation, distribution and handling vehicles environmental conditions. That, especially designed and conditioned vehicles were required to maintain fluctuations of temperature not exceeding 30°C to comply the WHO-EMRO Stability Guidelines. Dataloggers records can be an efficient tool to monitor the storage conditions for licensing a medicine storage facility.

Using Dataloggers method in calculating MKT of both transportation and storage conditions was justiceous for all over the world and greatly support the thought of globalization of drug stability guidelines. Conditions defined by WHO-EMRO for Sudan are to be follwed, howerver, zooning of countries should be based on the worst conditions.

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Software Programs

1. Datalogger for windows, SK-L 200 TH II, CD program, Sato- Japan. www.sksato.co.jp.
2. Stability System II software for Calculating the MKT, by Dr. Mike Yang, Scien Tek, USA. www.stabilitysystem.com.