

**INFLUENCE OF STORAGE CONDITIONS ON THE SHELF LIFE
OF CEPHALEXIN TABLETS STORED IN HOSPITAL AND
COMMUNITY PHARMACIES IN DIFFERENT PARTS OF KERALA.**

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ABSTRACT

Objectives: To determine the influence of storage conditions on the shelf life of Cephalexin stored in Hospital and Community Pharmacies situated in different parts of Kerala. **Methods:** Different brands of Cephalexin tablets were selected for this study. Samples collected from different time intervals were suitably coded and analyzed. **Results** Study was observed that, Mean Maximum Temperature was recorded more in Kannur (33.35⁰C) and Kozhikode (32.44⁰C) city as compare to Cochin (31.45⁰C). The Mean Relative Humidity was recorded more at Cochin (86.75%) as compared to Kannur (84.5%) and Kozhikode (84.58%). The study data show that percentage strength was least in samples collected from Cochin compared with those collected from Kozhikode and Kannur. Mean kinetic humidity was more in coastal

area, which may have accelerated the degradation of samples from Cochin. A significant statistical difference ($p= 0.0000$) was observed across brands. **Conclusions:** The study identifies the importance of storage conditions of antibiotics in pharmacies for better pharmaceutical care. Hence the regulatory authorities and pharmaceutical organizations should highlight the importance of maintaining good storage conditions in hospital and community pharmacies.

Key words: Shelf life, Storage, Regions.

INTRODUCTION

Pharmacy is the health profession that links the health sciences with the basic sciences; it is committed to ensuring the safe and effective use of medication. [1] Demographic and epidemiologic transitions have imposed demands on health service provision, as have health sector reforms, the challenges of aging populations, disease profiles, the changing pharmaceutical landscape, and new care models created to respond to changing disease patterns. These developments have had an impact on the different sectors of pharmacy. Pharmacy has moved from the historical orientation of product-focused service to patient-centered approaches. [2] The mission of pharmacy practice is to provide medications and other healthcare products and services and to help people and society to make the best use of them. All practicing pharmacists are obliged to ensure that the service they provide to every patient is of appropriate quality. Good pharmacy practice is a means of clarifying and meeting that obligation. [3] Pharmaceutical manufacturers determine a drug's shelf life or expiration date, through stability testing. This type of testing ensures that a drug's potency and integrity are intact over a specific amount of time, which becomes the expiration date. Several factors can influence these dates, including type of active ingredients, storage conditions, preservatives and what kind of container the drug will be stored in. It is important to note that the manufacturers' expiration dates apply only to the original packaging of the drug, and that once opened these dates no longer apply. [4]

Improper storage of the pharmaceutical products is one the fundamental concerns in patient care. This study emphasizes the importance of proper storage of pharmaceuticals from the time of their movement from manufacturing premises till it reaches the consumers. [5] The last leg of its journey at wholesale dealer's premises and retail outlets occupies a sufficiently long period of storage. Pharmaceuticals get exposed to varying temperature and humidity conditions during this part of movement, and with the prevailing conditions of the pharmacy outlets in India. Kerala is a tropical region and several places in the state are very hot and/or humid and at times with an intense light. Pharmaceutical products sometimes cannot remain stable in such conditions unless the labeled storage conditions on the products are adhered to. Accordingly, it becomes the duty of everybody in the distribution chain to value the storage conditions. The pharmacist in a pharmacy has the specific responsibility in this regards as the retention time of the product in the establishment is fairly long. This work will act as a guidance document for helping the community pharmacist and hospital pharmacist to recognize the importance of proper storage practices.

METHODS AND MATERIALS

Different brands of Cephalexin tablets were collected for this study from hospital and community pharmacies located in different regions of Kerala. Regions selected for study were Kannur, Kozhikode and Ernakulum (Cochin). Main reason for selecting these regions was convenience of collecting samples. Cochin is the largest city in Kerala and is located on the coast. Kozhikode is the capital of Malabar region of Kerala and has largest consumers for pharmaceuticals. Kannur was selected because it was nearest to the study center. The potency of the collected samples was estimated at different time intervals i.e. within six months of the date of manufacturing (Phase-I), after 6 months from date of manufacturing and before 6 months of date of expiry (Phase-II) and within 6 months of date of expiry (Phase-III). Samples collected from these intervals were suitably coded and analyzed (Table: 1). Human ethical clearance was obtained from Ethical Committee of Academy of Medical Sciences, Pariyaram Medical College, Kannur (*Order no: B2.9799/04/ACME dated on 19/04/2006*). All the analytical evaluations were done using UV spectrophotometric and HPLC method according to Indian Pharmacopoeia. [6, 7, 8]

RESULTS AND DISCUSSION

Shelf life is the capacity of a drug substance or drug product to remain within established specifications to maintain its identity, strength, quality, and purity throughout the retest or expiration dating periods. Physical, chemical, and microbiological data were generated as a function of time and storage conditions (e.g., temperature and relative humidity). [9] Pharmaceutical manufacturers determine a drug's shelf life or expiration date, through stability testing. This type of testing ensures that a drug's potency and integrity are intact over a specific period of time. Different brands of Cephalexin tablets were selected for the present study and selected antibiotic molecules were highly sensitive to temperature as well as humidity. There are more than 40 penicillins in clinical practice today and almost all of them follow the same degradation behavior at the beta-lactam moiety. Potency data of Cephalexin tablets from different regions of Kerala are shown in Table no 2. Data showed that percentage strength of Cephalexin was least in samples collected from Cochin compared with those collected from Kozhikode and Kannur. The climate of Kerala, as per Kerala State Council for Science, Technology and Environment [10], is tropical monsoon with seasonally excessive rainfall and hot summer. The entire state was classified as one meteorological sub division for climatologically purposes. The State is extremely humid due to the Arabian Sea in the west. As the State stretches from north to south with the Arabian Sea in its west, relative

humidity is in general high over the State. In the period January to March afternoon humidity reduces to 60 - 63%, varying from 35% in the interior to 71 % in the coastal area. The diurnal variation in relative humidity during this period is maximum and ranges from 4 to 16%, depending upon the proximity of the sea. The relative humidity in the monsoon period rises to about 85% for the state.

Table 1 Sample Coded For Analysis

Sampling Time	Sample code
I st Phase	A,B,C
II nd Phase	A1,B1,C1
III rd Phase	A2,B2,C2

It was observed that, there were seasonal fluctuations in the Mean Kinetic Temperature and Mean Kinetic Humidity in the various regions of Kerala. According to the meteorological data given by Indian meteorological department, the relative humidity in preferred region was high during the month of May to September. Temperature was found high during the period from January to April. Mean Maximum Temperature was recorded more in Kannur (33.35⁰C) and Kozhikode (32.44⁰C) city as compare to Naval Air Station (31.45⁰C), Kochi. The Mean Maximum Humidity was recorded more at Cochin (86.75%) as compared to Kannur (84.5%) and Kozhikode (84.58%). According to ICH guidelines, India comes under Zone III- hot, dry and Zone IV- very hot, moist. Zone III and IV have the Mean Kinetic Temperature of 30⁰C and yearly average humidity (% RH) were 35 and 70. These variations may be capable of influencing the shelf life of antibiotics. Mean Kinetic Humidity was observed more in Cochin region, which might accelerated the degradation of Cephalexin samples collected from Cochin. This influence of humidity was significantly less on samples collected from other regions. Praveen Khullar et.al [5] conducted a study on Temperature and Humidity mapping and real time, short term, on site, quality monitoring studies of four pharmaceutical formulations stored in chemist retail outlets in Delhi and result shows that comparatively higher fall in assay was observed in chemist outlets with moderate and poor storage facility as compared to those with good conditioning facility. Only good conditioned chemist outlets had an acceptable Mean Kinetic Temperature of around 25⁰C while those in poorly conditioned outlets exceeded 30⁰C. The lowest assay value being observed in warm zone of poorly conditioned pharmacies. The pharmaceutical products retained their potency when stored in pharmacies having good storage facility. There is a need for improving the storage

facility in pharmacies wherever the environmental controls are desired especially in summer months.

Table- 2 Percentage Potency Data of Cephalexin at Different Regions

Sample time	Sample NO	KANNUR [Amt (%)]	KOZHIKODE [Amt (%)]	COCHIN [Amt (%)]
FIRST (I)	A	270.08(108.03)	258.30(103.32)	266.93(106.77)
	B	260.37(104.14)	253.93(101.57)	250.18(100.07)
	C	262.63(105.05)	268.34(107.34)	259.73(103.89)
SECOND (II)	A1	251.63(100.65)	246.66(98.66)	242.18(96.87)
	B1	248.29(99.32)	242.79(97.12)	238.72(95.49)
	C1	253.04(101.22)	249.16(99.66)	241.08(96.43)
THIRD (III)	A2	224.42(89.77)	221.18(88.47)	198.53(79.41)
	B2	215.62(86.25)	209.83(83.93)	201.26(80.50)
	C2	212.19(84.87)	210.31(84.12)	183.59(73.44)

I. Within six month of date of manufacturing, II. After 6 month from date of manufacturing and before 6 month of date of expiry, III. Within 6 month of date of expiry.

The degradation occurs mainly because of the chemical reaction of the active ingredients or additives. Many drugs will react with atmospheric oxygen, so oxidation is a prime cause of degradation. [11] Degradation of many antibiotics follows first order kinetics and the rate concentration increases with an increases in temperature and. [12, 13] According to R.A.Lowe [14] 10% degradation of drugs was relevant with regards to the effect of temperature conditions. M. Córdoba-Borrego & Di'az. [15] and M. Córdoba, M. Cordoba & Di'az. [16] explained that Norfloxacin was photosensitive and hygroscopic [17] Drug may prolong exposure to direct sunlight results in the formation of different degradate. World Health Organization, 1996 defines the mission of pharmacy practice as “to provide medications and other healthcare products and services and to help people and society to make the best use of them”. According to International of Health care Research, 2001 the “use of pharmaceutical not only deals with pharmacological issues. The conditions of safe, effective and affordable medicinal drugs of good quality and in the right quantity to the whole population and used rationally and appropriately, should be a priority in health and drug policies”. Evaluation made during the study provides significant evidences that the quality of an antibiotic under the influence of various environmental factors may change with time. Maintaining proper storage conditions at hospital and community pharmacies is essential to reduce such impact caused by environmental factors. The pharmaceutical products were found to retain their potency when stored in pharmacies having good storage

facilities. Hence the regulatory authorities and pharmaceutical organizations should highlight the importance of maintaining good storage conditions in hospital and community pharmacies functioning in the study regions of Kerala.

CONCLUSION

Storage of drug products is an important requisite in efficient pharmacy practices. Optimum storage conditions and procedures ensure that the potency and integrity of medicinal products are maintained throughout their shelf life. Chief pharmacist should ensure that the Standard Operating Procedure (SOP) is followed in their pharmacies. Pharmacy staff and other personnel involved in storage must follow the SOP without deviation. Kerala is a tropical region and several places in the state are very hot and/or humid and at times have intense light. In such conditions the antibiotics sometimes cannot remain stable unless the labeled storage conditions on the products are adhered to. Accordingly, it becomes the duty of the pharmacist working in hospital and community pharmacy to adhere to the storage conditions.

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