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Optimization of Gas Exposure Time for Ethylene Oxide (ETO) Sterilization

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Abstract: ***Advancement in technology made the medical device manufacturing industry prominent among all the industrial sectors. Most health care products and medical devices require sterilization. Due to the heat sensitivity of the medical devices, Ethylene Oxide (ETO) sterilization is recommended but ETO is an expensive and long process. Now, there is a need to find an efficient, minimal cost and a lesser amount of time for sterilization process. In this present study, we developed and validated a minimum time, low cost, and efficient ETO sterilization process that can be used at an Industrial scale.***
Keywords: ETO Sterilization, Gas sterilization, Effect of time, Optimization of Gas, Exposure time.

I. INTRODUCTION

In the Medical Devices and Health care sector, sterilization has become more sophisticated owing to the necessity to prevent the patient's exposure to infectious organisms on the Medical, Health care products and Devices. Inadequate sterilization of these materials/products can lead to substantial institutional costs associated with the patient's nosocomial infections and mortality concerns[1]. This can be prevented by implementing proper disinfectants and sterilization practices.

Medical devices incorporate all forms of tools or equipment engaged in the diagnosis, detection, contraception, and treatment of physiological conditions of the human body, playing a prominent role in the well-being of humans either in contact or non-contact ways[2].

The Ethylene oxide (C_2H_4O) is a colourless, odourless[3],volatile molecule with boiling point of 10.4 °C at 760 mm Hg[4]. It is also referred as Oxirane or Epoxyethane[2]. In gaseous form, it acts as an excellent sterilization agent due to its bactericidal, sporicidal, and virucidal activity[1] with high-level reactivity, diffusivity. This microbicidal action[5] is through alkylation of cellular constituents such as functional proteins, enzymes, nucleic acids (DNA, RNA), by binding to the sulfhydryl (SH), hydroxyl (OH), amino (NH_2), and carboxyl (COOH) groups. This hinders the organism's regular cellular metabolism and its ability to proliferate, thus makes them non-viable[1]. This alkylation property of ETO does not require any metabolic activation and is irretrievable, hence it is used extensively as a Sterilant.

ETO sterilization is a low-temperature process hence extensively applied for the sterilization of Medical and Health care products that are heat sensitive. Other sterilisation techniques such as Steam, Dry heat sterilization techniques involve high temperatures of 121°C and 160°C respectively[6] makes them incompatible in treating such materials. Besides these, Irradiation sterilization can cause degradation of materials due to temperature effect and the energy of γ radiation has five times greater magnitude than a carbon chemical bond. This made ETO sterilization to be widely acceptable when compared to other sterilization processes in the Medical and Health care sector.

II. MATERIALS

A. ETO Sterilization Unit

An Industrial-scale Ethylene Oxide sterilization facility was set up at STERILA, in Andhra Pradesh Med Tech Zone (AMTZ) Campus, Visakhapatnam, Andhra Pradesh. The facility is accredited with ISO 13485:2016 and ISO 11135:2014. The sterilization chamber volume at our facility is approximately 550 cubic feet.

B. Raw Materials

Polytetrafluoroethylene (PTFE), Perfluoro alkoxy (PFA), Polyamides (e.g., Nylon), Polycarbonates (PC), Polythene (PE), Polypropylene (PP) stabilized, Polyvinyl chloride (PVC), Silicone adhesives, Cellulose ester, cellulose, paper, cardboard are the materials which can be processed for ETO sterilization.

C. Other Requirements

Ethylene oxide gas, Water, Electricity, Sterilization Indicators- Chemical and Biological Indicator (*Bacillus atrophaeus*, ATCC 9372), Medical Packaging roll/self-seal pouches.

D. Gas Composition

Ethylene Oxide gas used is mostly a mixed gas as a combination with inert gases like Carbon dioxide (CO_2) or Hydrochlorofluorocarbons (HCFC), or Nitrogen (N_2). The common blends used in most of the ETO sterilization studies include 100 wt.% ETO with/ without N_2; ETO(8.6-10wt.%) with CFC(90-91.4 wt.%); ETO(8.5-90 wt.%) with CO_2(10-91.5 wt.%) [6][7][8][9]. 100 wt.% ETO is not usually preferred as it is highly toxic and with a greater risk of explosion. Whereas HCFC's are susceptible to cause depletion of the ozone layer, due to which usage has been reduced. Nowadays CO_2 is the best alternative for combination with ETO as it is environment friendly and cost-effective when compared with other gases. At STERILA (ETO sterilization facility) …, we have used ETO and CO_2 blend with the composition of 90 v% and 10 v% respectively.

E. Phases of ETO Sterilization Process

A typical Ethylene Oxide sterilization process comprises three phases which include, Pre-conditioning, Gas exposure, and Aeration[10]. The Ethylene oxide sterilization cycle flow is depicted in ***Figure.1***.

1) *Pre-conditioning:* Before the Ethylene oxide administration, we ensure to attain a predetermined temperature, pressure (negative), and relative humidity. All these parameters are achieved during the preconditioning phase.
2) *Exposure Time:* The time for which the materials to be sterilized are exposed to ETO gas, immediately after gas injection is referred as ETO exposure time. The ETO gas acts on the materials, thereby killing viable microbial population making them sterile.
3) *Aeration:* A part of the sterilization process during which the ethylene oxide and by-products formed during the ETO cycle, desorb from the processed materials until pre-determined levels are achieved.

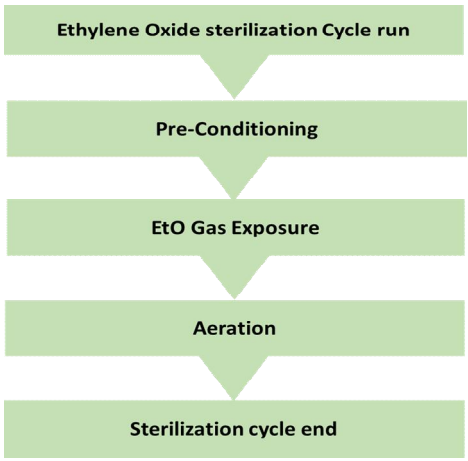


Figure.1. ETO sterilization process cycle flow diagram.

III. EXPERIMENTAL PROCEDURE

Ethylene oxide sterilization involves multiple parameters in the sterilization process which can alter the efficacy of the sterilization process. Each parameter can be modified based on the product compatibility, making ETO sterilization flexible. this affects the other dependent parameters contemplating the product compatibility with increasing the efficacy of the sterilization. These variables are summarized below.[1][8][4][5][7][11][12] [13]

A. Pressure

The ETO sterilization process completely occurs under complete vacuum (negative pressure). This hinders the sterilization efficacy as the air present in the load interferes with diffusion of moisture and affects heat and gas transfer inside the product. In addition, the process strategy also entails the gas injection and evacuation rates owing to an impact on sterilization lethality, while at the same time can cause a potential damage for package and to the product.

B. ETO Gas Concentration

Literature review have shown that, at an industrial scale ETO exposure time range from 6 to 24 h. At higher gas concentration levels, the sterilization can be achieved even under reduced cycle duration. However, high concentrations lead to increased ETO residual levels. This causes a necessity to increase aeration time. Gas concentration influences the microbial inactivation and with outgassing, and the optimization of the process needs to take the material into consideration i.e., absorption and retention.

C. Temperature

The temperature has a substantial microbicidal effect and can alter the ETO diffusion through cell walls and packaging materials. Lots with high density and low thermal diffusivity materials require a longer time to heat up. The mortality rate of the micro-organisms is dependent on the temperature and, therefore, if high temperatures are used, the cycle period may be reduced. Still, it is essential to consider the maximum temperature the product and the package can tolerate. The typical ETO sterilization cycle operates under 30-70 °C temperature.

D. Relative Humidity

Relative humidity plays a key role in EO sterilization and is most complex of the controllable variables. This is because it can alter ETO gas diffusion. Inadequate humidification can lead to failure of the sterilisation process in which SAL cannot be achieved. A relative humidity (RH) of range 30-80% (in the chamber) is commonly employed to achieve an effective ETO sterilization.

This process of sterilization is flexible, which outcomes from various parameters such as gas concentration, temperature, Exposure time or aeration time which can be altered based on the nature of the material to be sterilized to maintain the integrity of the material or device [1].

It is known that, with the increase in gas concentration, the exposure time can be reduced[14]. To test this phenomenon, we had carried out a set of ETO Sterilization cycles with a fixed gas concentration of 900mg/L, at a variable exposure time of 360min, 480min, 540min, 600min separately. The parametric data of all the ETO sterilization test cycles performed had been listed in ***Table.1***. By this test method, we can thereby conclude the minimum exposure time required to achieve the Sterility Assurance Level (SAL) at a higher gas concentration of 900mg/L.

IV. ETHYLENE OXIDE STERILIZATION VALIDATION

The effectiveness of a sterilization processes should be validated for sterility assurance. This process starts with commissioning, supported by Performance Qualification (PQ). Commissioning deals with that the validating the Operational specifications of the sterilization equipment intended for use and will function as per required parameters to achieve sterilization. This process qualification is validated by obtaining, documenting, and interpreting the results proving predetermined specifications are met. Performance qualification includes Physical performance qualification (PPQ) and Microbial performance qualification (MPQ). PQ uses the product that is to be sterilized to identify whether the instrument is operating in accordance with the acceptance criteria meeting the intended Sterility Assurance Level (SAL). Biological and Chemical indicators complying ISO standards are used as a part of PQ

The MPQ of ETO sterilization is validated through Half-cycle or Overkill approach employing *Bacillus atrophaeus* Biological Indicators (BI's). This demonstrates the lethality of the sterilization process.

In this study we have deployed Half cycle approach in which we performed three consecutive trails of sterilization with minimum of five Biological Indicators in random places inside the sterilizer within the lot. All the critical parameters are maintained constant all over the cycles except the ETO exposure time.

S.no	Gas Concentration	Temperature	Exposure time	Cycle No.
1.	900 mg/L	40-45^{o}C	600 mins (10 hours)	Cycle 1.1
				Cycle 1.2
				Cycle 1.3
2.	900 mg/L	40-45^{o}C	540 mins (9 hours)	Cycle 2.1
				Cycle 2.2
				Cycle 2.3
3.	900 mg/L	40-45^{o}C	480 mins (8 hours)	Cycle 3.1
				Cycle 3.2
				Cycle 3.3
4.	900 mg/L	40-45^{o}C	360 mins (6 hours)	Cycle 4.1
				Cycle 4.2
				Cycle 4.3

Table.1. Parametric Data of the ETO Sterilization test cycles performed, with a fixed gas concentration of 900 mg/L, at the different exposure times i.e., 600 min, 540 min, 480 min, and 360 min.

V. ETHYLENE GLYCOL (EG)

Ethylene glycol (C2H6O2) is clear, odourless, and colourless syrup like liquid with a sweet taste. It has low volatility and is miscible with water and some other solvents[15]. EG has many uses, including antifreeze in cooling and heating systems, automobiles, in hydraulic brake fluids, as an industrial humectant and also used to de-ice airport runways and aircrafts[16]. Limited data is available on measured concentrations of EG in environmental compartments. It has lower toxicity to aquatic organisms with a toxicity threshold ranging from 1000-6500 mg/m^3[15]. The EG is produced as a by-product of ETO sterilization upon reaction with water during aeration process[17]. The resultant EG is diluted with water to ensure the acceptable limits are achieved. In case of high pH of the effluent, it is treated with NaOH to neutralize its pH. This treatment if performed in the Effluent Treatment Plant (ETP). Once the treatment process is complete, the effluent can be drained into sewage[18].

VI. RESULTS AND OBSERVATION

ETO sterilization cycles with the gas concentration of 900mg/L and exposure time of 600 min, 540 min, 480 min, and 360 min were performed separately. A set of 3 cycles were runed for each period of exposure and passed on for sterility and validation check of the sterilization process. A total of 12 cycles was performed to validate this study. An overall cycle parameters response concerning time in the Exposure phase were plotted in ***Figure. 3.1-3.2.***

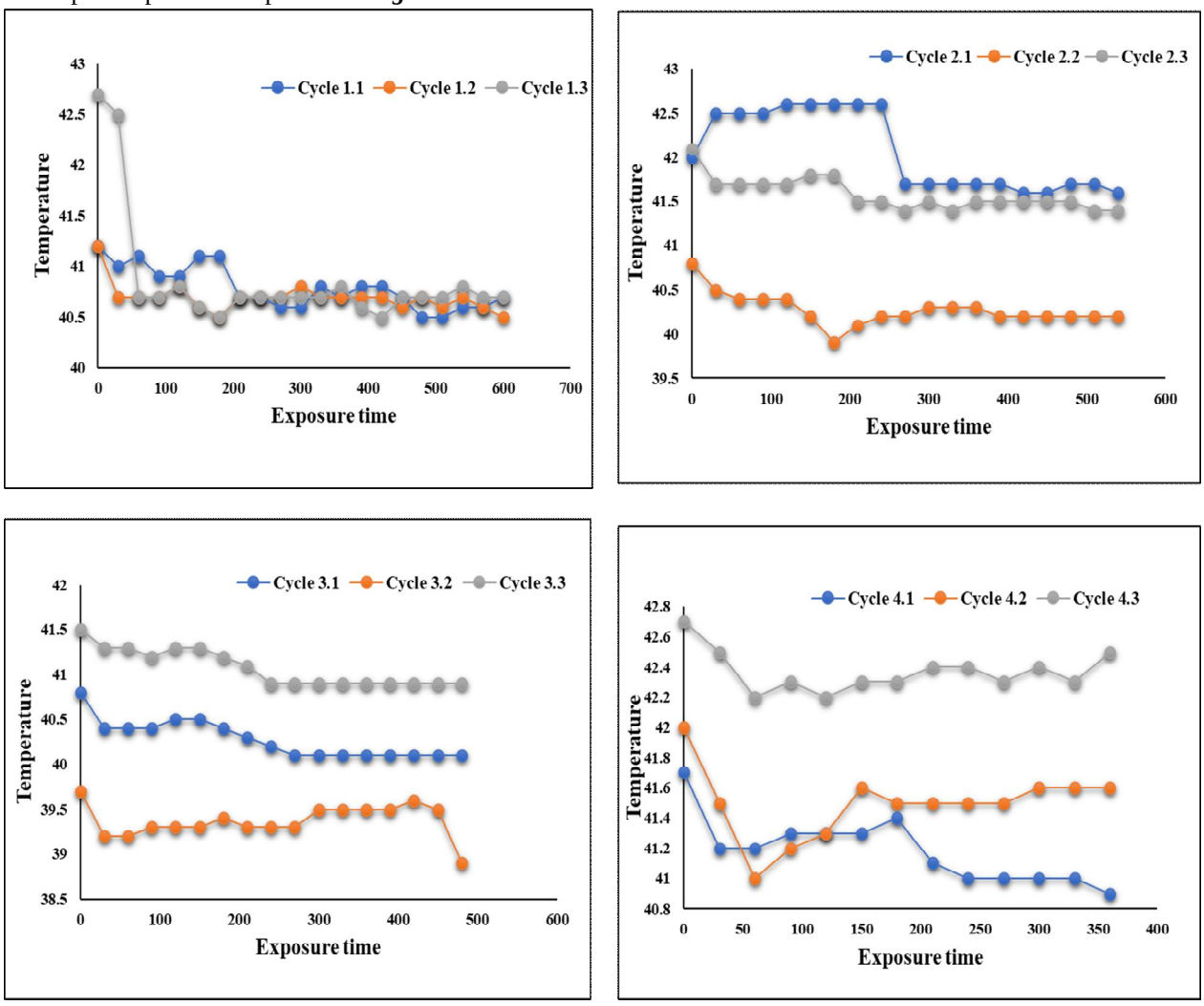


Figure.3.1. Temperature response with respect to ETO exposure time

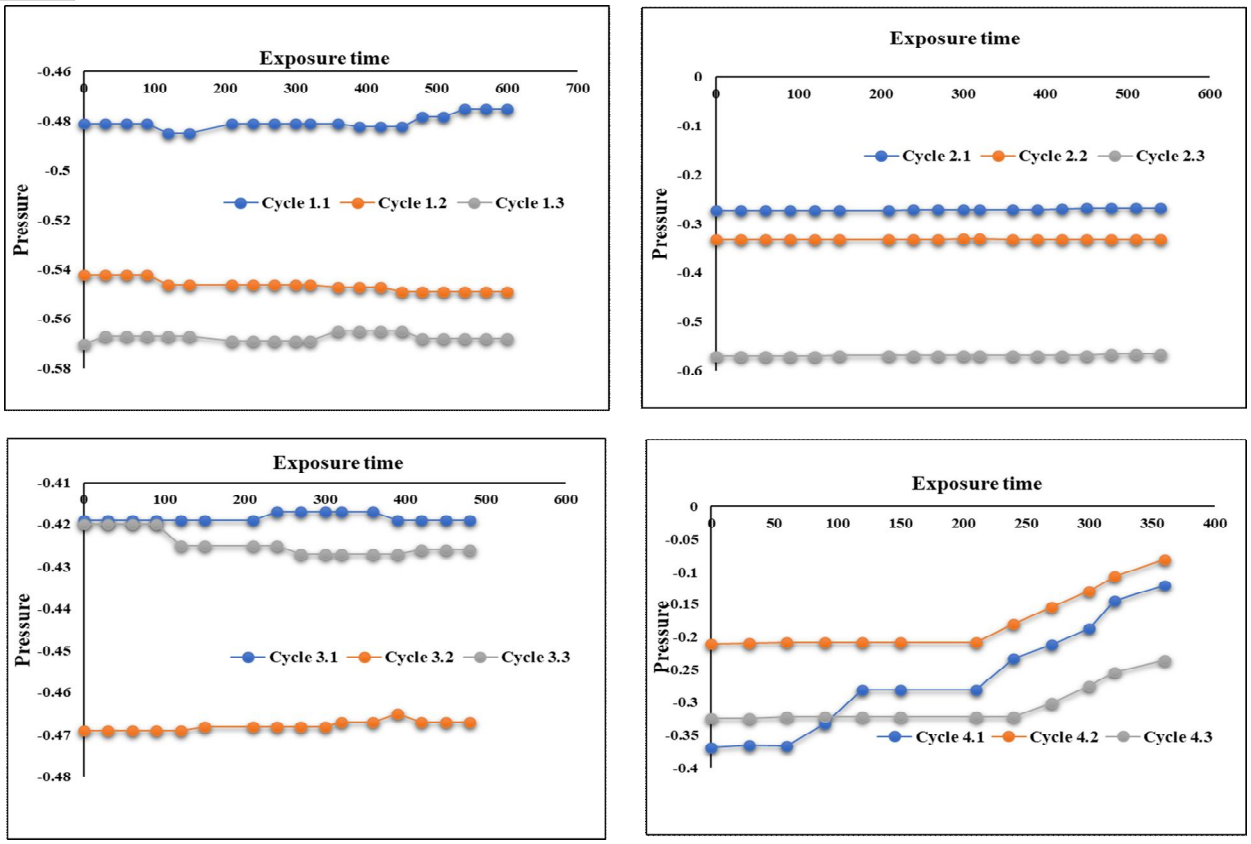


Figure.3.2. Pressure response with respect to ETO exposure time

Biological indicators placed withing the sterilization lot, had been collected post sterilization processes, media ampule is broken and incubated at 37^{o}C for a period of 14 days and there were no signs of microbial growth.

VII. CONCLUSION

Biological Indicators data stating absence of any Microbial growth post 14-day incubation proven that the SAL has been achieved at all the exposure times. These results conclude that the sterility achieved at 900mg/L gas concentration at exposure time ranging from 600 min to

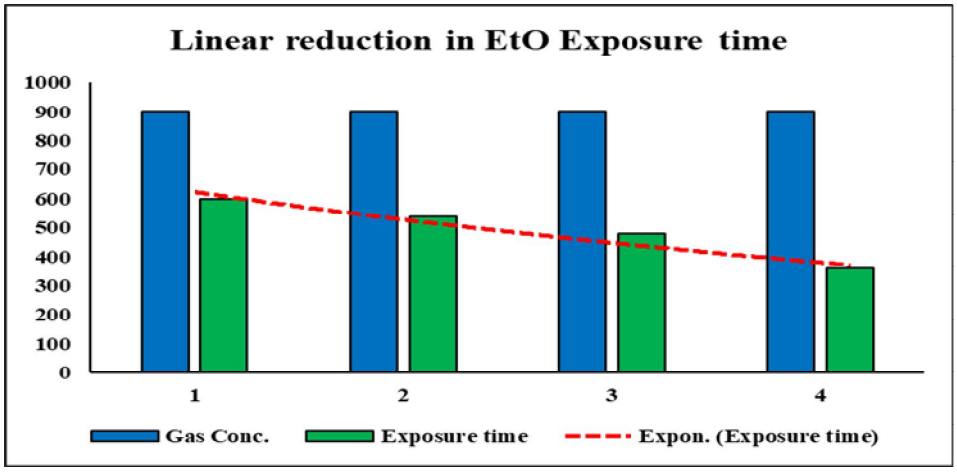
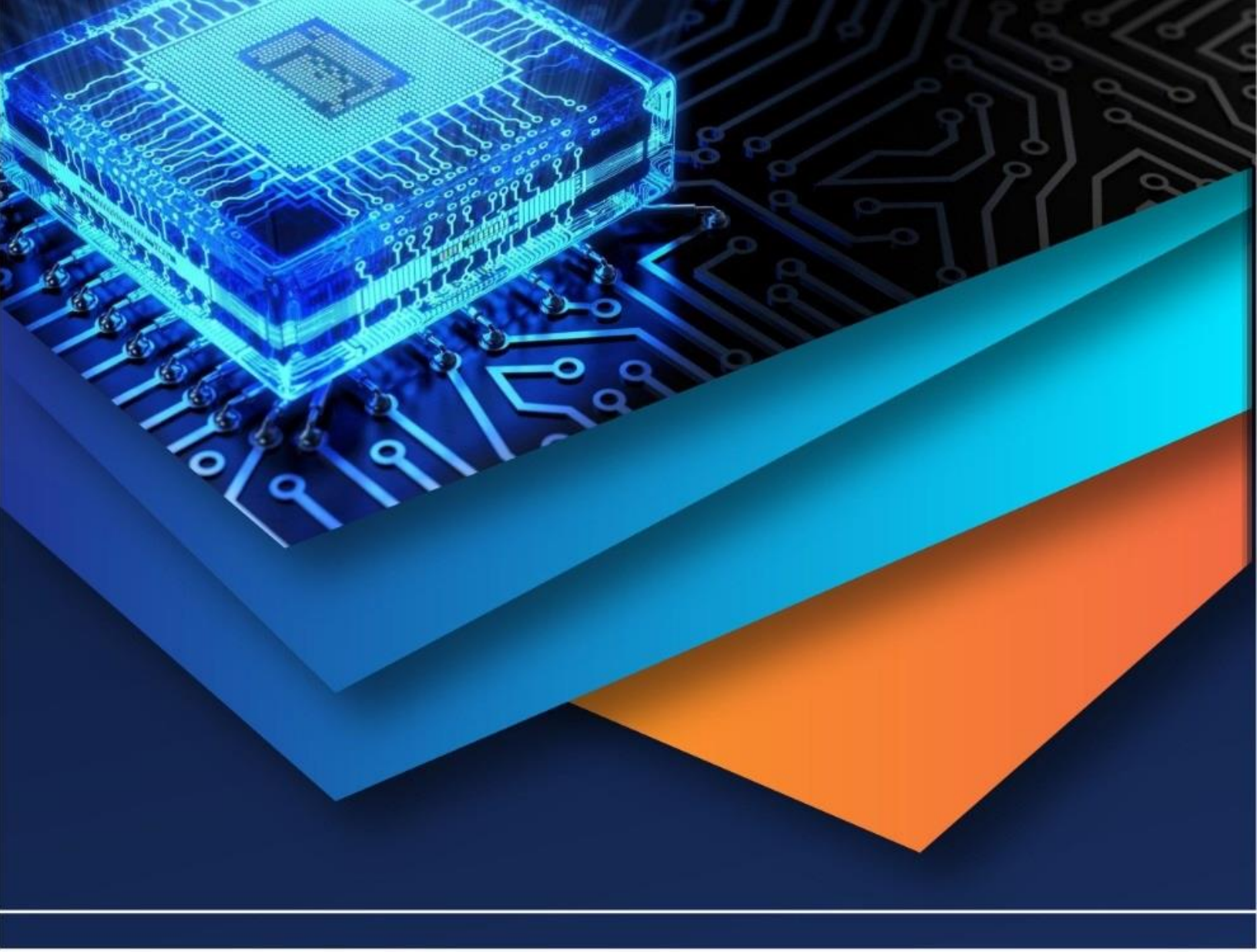


Figure.3.3. Linear reduction in exposure time under constant ETO gas concentration.

360 min. By the above observations the products are sterilized even at minimum exposure time of 360 min which proves our statement that “With increase in ETO gas concentration, Exposure time can be reduced” but this reduction in exposure time maintains the SAL post sterilization.

REFERENCES

[1] G. C. C. Mendes, T. R. S. Brandão, and C. L. M. Silva, "Ethylene oxide sterilization of medical devices: A review," Am. J. Infect. Control, vol. 35, no. 9, pp. 574–581, 2007, doi: 10.1016/j.ajic.2006.10.014.
[2] L. S. Sreejith and R. Sasi, "Residual ethylene oxide in medical devices: Effects and estimation methods, an overview," Trends Biomater. Artif. Organs, vol. 34, no. 1, pp. 7–12, 2020.
[3] J. Brooksbank, "Public Health vs. Public Health: Balancing Environmental Concerns with the Need for Sterile Medical Devices," Minnesota J. Law, Sci. Technol., vol. 21, no. 2, p. 441, 2020.
[4] N. P. Tipnis and D. J. Burgess, "Sterilization of implantable polymer-based medical devices: A review," Int. J. Pharm., vol. 544, no. 2, pp. 455–460, 2018, doi: 10.1016/j.ijpharm.2017.12.003.
[5] M. P. Nikolova, V. Nikolov, S. Valkov, E. Yankov, V. Zaharieva, and P. Petrov, "Ethylene oxide sterilization of TiN/TiO2 coated titanium implant material," Key Eng. Mater., vol. 813 KEM, pp. 178–184, 2019, doi: 10.4028/www.scientific.net/KEM.813.178.
[6] S. Govindaraj and M. S. Muthuraman, "Systematic review on sterilization methods of implants and medical devices," Int. J. ChemTech Res., vol. 8, no. 2, pp. 897–911, 2015.
[7] D. K. Gilding, A. M. Reed, and S. A. Baskett, "Ethylene oxide sterilization: effect of polymer structure and sterilization conditions on residue levels," Biomaterials, vol. 1, no. 3, pp. 145–148, 1980, doi: 10.1016/0142-9612(80)90037-X.
[8] G. C. Mendes, T. R. S. Brandão, and C. L. M. Silva, Ethylene oxide (EO) sterilization of healthcare products. Elsevier Masson SAS., 2012.
[9] D. Niosh and P. Number, "The National Institute for Occupational Safety and Health Ethylene Oxide Sterilizers in Health Care Facilities : Engineering Controls and Work Practices Current Intelligence Bulletin 52," 1989.
[10] L. Chen, "Improving Microbiological Safety of Low Moisture Food Products Using Radio Frequency and Ethylene Oxide," ProQuest Diss. Theses, p. 229, 2020, [Online].
[11] R. E. Harrington, T. Guda, B. Lambert, and J. Martin, Sterilization and Disinfection of Biomaterials for Medical Devices, Fourth Edi. Elsevier, 2020.
[12] B. M. Su-Velez, T. Maxim, J. L. Long, M. A. St John, and M. A. Holliday, "Decontamination Methods for Reuse of Filtering Facepiece Respirators," JAMA Otolaryngol. - Head Neck Surg., vol. 146, no. 8, pp. 734–740, 2020, doi: 10.1001/jamaoto.2020.1423.
[13] I. Aguado-Maestro, M. De Frutos-Serna, A. González-Nava, A. B. Merino-De Santos, and M. García-Alonso, "Are the common sterilization methods completely effective for our in-house 3D printed biomodels and surgical guides?," Injury, no. xxxx, pp. 1–5, 2020, doi: 10.1016/j.injury.2020.09.014.
[14] M. Busters, "Ethylene Oxide Gas Ethylene Oxide Gas," no. 2008, pp. 873–874, 2000.
[15] S. Dobson, "Concise International Chemical Assessment Document 22: Ethylene glycol: Environmental aspects," IPCS Concise Int. Chem. Assess. Doc., no. 22, 2000.
[16] H. Summary, "Ethylene Glycol Hazard Summary," no. 3, pp. 3–6, [Online]. Available: https://www.epa.gov/sites/production/files/2016-09/documents/ethylene-glycol.pdf.
[17] D. Pont, "Material Safety Data Sheet Material Safety Data Sheet," vol. 4, pp. 1–5, 2010.
[18] A. Gasc et al., "No 主観的健康感を中心とした在宅高齢者における 健康関連指標に関する共分散構造分析Title," Photosynthetica, vol. 2, no. 1, pp. 1–13, 2018, [Online].



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