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Compiled by
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Lockheed

MISSILES & SPACE COMPANY
A GROUP DIVISION OF LOCKHEED AIRCRAFT CORPORATION
SUNNYVALE, CALIFORNIA

ABSTRACT

Ethylene oxide has proven to be one of the better agents for the sterilization of spacecraft. The scope of this search involves the chemical reactions involved in the destruction of microorganisms and their spores.

The 39 references which were selected are alphabetically arranged according to the first author. The resources of the LMSC Technical Information Center were utilized in this search.

The period of coverage dates from 1950 to June 1962.

Search Completed July 1962.

Availability notices and procurement instructions following the citations are direct quotations of such instructions appearing in the source material announcing that report. The compiler is well aware that many of these agencies' names, addresses and office codes will have changed; however, no attempt has been made to update each of these notices individually.

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This selective bibliography has been prepared in response to a specific request and is confined to the limits of that request. No claim is made that this is an exhaustive or critical compilation. The inclusion of any reference to material is not to be construed as an endorsement of the information contained in that material.

TABLE OF CONTENTS

1. Alexander, P.

Formation of new cross-linking bridges in fibers and possible physiological effects of some chemicals used for this purpose.

MELLIAND TEXTILBER v. 35, p. 3-9, 1954.

Discusses ethylene oxide along with a number of other alkylating compounds in relation to their effects on wool. The author links the chemical activity of ethylene oxide to its growth retarding action.

2. Allen, R.C.

Ethylene glycol produced by ethylene oxide sterilization and its effect on blood-clotting factors in an inbred strain of mice. NATURE v. 193, p. 387-8, 27 Jan 1962.

3. Barber, E. and Flynn, P.

ASTRONAUTICS INFORMATION. EFFECTS OF STERILIZING AGENTS ON MICROORGANISMS. Jet Propulsion Lab., Calif. Inst. of Tech., Pasadena. Literature search no. 260, Aug 61, 55p. (Contract NASw-6) ASTIA AD-264 023.

Material has been collected on the effect of sterilizing agents on bacteria, spores, and viruses, and on the production and maintenance of sterile environments in the laboratory. There is a section for each type of sterilizing agent: radiation, temperature, ultrasonics, and vacuum. Radiation is divided into gamma-, ultraviolet-, and X-radiation, and the section on vacuum contains material on the effects of drying. An author index is included. In each section, the material is divided into books, reports, and periodicals. Books are arranged in alphabetical order by author, and reports by source. Periodicals are arranged by year with most recent material first, and within each year in alphabetical order by journal name. Abstracts found in the reference source are published here in whole or in part, and the source is noted whenever possible.

4. Blackwood, J.D. and Erskine, E.B.
Carboxide poisoning. U.S. NAVAL MED. BULL.
v. 36, p. 44-5, 1938.

Carboxide is a trade name for ethylene oxide.

5. Bruch, C.W.
Gaseous sterilization. ANN. REV. MICROBIOL.
v. 15, p. 245-62, 1961.

A review with 262 references.

6. Castrén, O. and Raunio, V.
The viricidal action of ethylene oxide. Experience gained by methods employing tissue culture for control of the results. ANN. MED. EXPL. ET BIOL. FENN. v. 38, p. 16-20, 1960. (In English)

7. Davies, R.W. and Comuntzis, M.G.
THE STERILIZATION OF SPACE VEHICLES TO PREVENT EXTRATERRESTRIAL BIOLOGICAL CONTAMINATION. Jet Propulsion Laboratory, California Institute of Technology, Pasadena. External publication 698. Presented at the Tenth Annual Congress of the International Astronautical Federation, London, 30 Aug – 5 Sep 1959.

It is possible to prevent earthly organisms from contaminating the moon and planets, but careful planning will be required. Methods of sterilization include the use of ethylene oxide, heat and radiation, and the sterile assembly of special components.

8. Diding, N.

Some observations on the sterilizing effect of ethylene oxide. SVENSK. FARM. T. v. 64, p. 713-9, 10 Oct 1960.

9. Diding, N.

Some observations on the sterilizing effect of ethylene oxide. PHARM. ACTA HELV. v. 35, p. 582-7, Nov 1960.

10. Dosch, F.

The germicidal effectiveness of ethylene oxide – carbon dioxide in comparison to that of steam. ZBL. BAKT. [ORIG.] v. 184, p. 201-3, Jan 1962. (In German)

11. Fraenkel-Conrat, H. L.

Action of 1, 2-epoxides on proteins. J. BIOL. CHEM. v. 154, p. 227-38, 1944.

Demonstrates that alkylating agents (including ETO) can attack the -COOH, $-NH_2$, -SH, and -OH groups of protein. It is felt that the radicle groups are replaced by $-CH_2CH_2OH$ groups, thus blocking essential metabolic reactions.

12. Jacobson, N.F.

THE OPERATIONS PROBLEM OF STERILIZATION. Jet Propulsion Laboratory, California Institute of Technology, Pasadena. Presented at the American Rocket Society Missile and Space Vehicle Testing

12. (cont'd) Conference, Los Angeles, Calif., 13-16 Mar 1961.
(American Rocket Society, Inc., New York, N.Y.
1671-61.)

The proposed procedures for the sterilization of a spacecraft are described.

13. Kaye, S.
The sterilizing action of gaseous ethylene oxide.
III. The effect of ethylene oxide and related compounds upon bacterial aerosols. AM. J. HYGIENE
v. 50, p. 289-95, 1949.

Describes the experimental procedures and results. Ethylene oxide and its derivatives were found to be less bactericidal than ethylene imine and its derivatives.

14. Kaye, S. and Phillips, C.R.
The sterilizing action of gaseous ethylene oxide.
IV. The effect of moisture. AM. J. HYGIENE
v. 50, p. 296-306, 1949.

A consideration of the role of moisture in the sterilizing qualities of ethylene oxide. The authors feel that ethylene oxide is most effective in a dry atmosphere. Under super-dry conditions this effect is reversed. The reversed effect is related to concentrations of gas and atmospheric moisture will be affected by the amount of both present.

15. Kelsey, J.C.
Sterilization by ethylene oxide. J. CLIN. PATH.
v. 14, p. 59-61, 1961.

A general description of ethylene oxide and its applications. There is an inference that its bactericidal effect is due to its alkylating characteristics.

16. Kowalik, R. J. and Sadurska, I.

Effect of ethylene oxide on some wood-destroying fungi. Inst. Przemyslu Org., Warsaw. ACIA MICROBIOL. POLON. v. 9, p. 67-9, 1960. (In Polish)

The fungicidal action of a 10:90 mixture of ethylene oxide and CO_2 was demonstrated on Coniphora cerebella, Poria vaporaria, Merulius domesticus, and Polyporus versicolor grown on wooden blocks. Polyporus versicolor was the most resistant.

17. Krylova, N. A.

Determination of ethylene oxide in the air. GIG. SANIT. v. 26, p. 48-9, Oct 1961. (In Russian)

18. Liebermeister, K.

On evaluation of steam and gas sterilizers. ZBL. BAKT. [ORIG.] v. 184, p. 181-201, Jan 1962. (In German)

19. Maron, N.

The rigidity of gelatin gels as influenced by inactivation of selected reactive groups. Soc. An. Gelatine, Hasselt, Belg. ADHASION v. 3, p. 553-7, 1959.

The treatment of gelatin powder with diazomethane, ketene, or ethylene oxide at room temperature for 24 hours reduced the rigidity of the gel, increased its viscosity, and raised its isoelectric point. The reasons for these responses are discussed.

20. Mergenhagen, S.E., Scott, D.B. and Scherp, H.W.
Lysis by human oral bacteria of collagen altered by ethylene oxide. Natl. Inst. of Dental Health, Bethesda, Md. PROC. SOC. EXPTL. BIOL. MED. v. 103, p. 227-9, 1960.

Treatment of reconstituted collagen with ethylene oxide renders it more digestible by certain human oral strains of bacteria. Electron micrographs reveal the absence of typical cross-striated fibrils in the ethylene oxide treated collagen. A loose net of finer unstriated fibrils was present.

21. Opfell, J.B., Hohmann, J.P. and Latham, A.B.
Ethylene oxide sterilization of spores in hygroscopic environments. Cutter Labs., Berkeley, Calif. J. AM. PHARM. ASSOC., SCI. ED. v. 48, p. 617-19, 1959.

Environmental hygroscopic substances such as glycerine or filter paper increases the resistance of spores of Bacillus globigii to the sterilizing action of ethylene oxide.

22. Phillips, C.R. and Kaye, S.
The sterilizing action of gaseous ethylene oxide. I. Review. AM. J. HYGIENE v. 50, p. 270-9, 1949.

A review of ethylene oxide, its applications, and its merits.

23. Phillips, C.R.
The sterilizing action of gaseous ethylene oxide. II. Sterilization of contaminated objects with ethylene oxide and related compounds: Time,

23. (cont'd) concentration and temperature relationships.

AM. J. HYGIENE v. 50, p. 280-8, 1949.

The coefficient of dilution of ethylene oxide is close to unity. The temperature coefficient is 2.74 for each 10° C rise. Other compounds containing the same epoxy groupings have also been shown to possess bactericidal properties as do compounds containing the 3-membered ethylene sulfide or ethylene imine rings. The effects of ethylene oxide are considered to be related to its alkylating effects.

24. Phillips, C.R.

Relative resistance of bacterial spores and vegetative bacteria to disinfectants. BACT. REV. v. 16, p. 135-8, 1952.

The author links the action of ethylene oxide to its alkylating activity.

25. Phillips, C.R. and Hoffman, R.K.

Sterilization of interplanetary vehicles.

SCIENCE v. 132, p. 991-995, 14 Oct 1960.

Sterilization of interplanetary vehicles was investigated to find out primarily whether: (1) contamination should be avoided; (2) if all life forms would be automatically killed in passage because of the rigor of interplanetary space; and (3) if sterilization can be accomplished without adding crippling restrictions to the space exploration program. Results were as follows: (1) contamination should be avoided to enable man to examine habitat life forms other than those which arose on earth; (2) since microorganisms could probably well withstand space flights, space vehicles should be sterilized before leaving the earth to avoid living earth forms from being transported to other celestial bodies; and (3) design consideration and laboratory experiments indicated that chemical sterilization with ethylene oxide promises a good solution because it's easily stored with fluorohydracarbons in lightweight containers, and the fact that fewer types of materials are damaged by this technique than any known sterilization method. Should, however, some component prove sensitive to ethylene oxide, it could be sterilized prior to assembly by another technique and shielded from further exposure by building a gas-tight barrier around it. This method also adopts itself to simple exposure chambers; for example, a simple polyethylene bag tightly closed at the neck would serve adequately as a device to contain the gas. Objects of any size could be sterilized by building about them a bag or tent of heat-sealed plastic sheeting and admitting the sterilized mixture into this container. A hypothetical case is given of a space vehicle atop a third-stage rocket with both of them covered by a nose cone or fairing, wherein ethylene oxide provides sterilization for both the vehicle and each rocket stage.

26. Posner, J. (ed.)

PROCEEDINGS OF MEETING ON PROBLEMS AND TECHNIQUES ASSOCIATED WITH THE DECONTAMINATION AND STERILIZATION OF SPACECRAFT, JUNE 29, 1960, WASHINGTON, D.C.

National Aeronautics and Space Administration, Washington, D.C. Jan 1961, 57p. ASTIA AD-248 765. (Also Available from NASA, Washington, D.C., as NASA Technical Note D-771)

A meeting was held of representatives of agencies concerned with the development of space vehicles and those investigating decontamination and sterilization procedures. Recommendations resulting from the deliberations include: (1) a body of related information be accumulated, (2) standard operating procedures be established, (3) acceptable limits of contamination be determined, (4) NASA policy be clarified, (5) new sterilizing agents be developed, (6) compatibility studies be pursued, (7) sterile manufacture of parts be investigated, and (8) a working level group should be formed to implement recommendations and procedures.

27. Raunio, V. and Taipale, A.

The action of ethylene oxide on polio virus adsorbed on HeLa cells. Removal of gas after treatment of cell cultures with ethylene oxide.

ANN. MED. EXP. ET BIOL. FENN. v. 39, p. 352-5, 1961.

28. Reddish, G.F. (ed.)

Antiseptics, disinfectants, fungicides, and chemical and physical sterilization. Philadelphia, Lea and Febiger, 1957.

28. (cont'd) The chapter titled "Gaseous Sterilization" by C.R. Phillips discusses ethylene oxide (ETO). The mechanism by which ETO kills microorganisms has been linked to its chemical activity as an alkylating agent. According to the alkylation theory, ETO replaces labile hydrogen atoms with hydroxyl ethyl groups, thus blocking many reactive groups needed in essential metabolic reactions.

29. Royce, A. and Bowler, C.

Ethylene oxide sterilization – some experience and some practical limitations. J. PHARM. PHARMACOL. v. 13 (Suppl.), p. 87-94, Dec 1961.

30. Tessler, J., et al

The inactivation of foot and mouth disease virus with liquid ethylene oxide. AM. J. VET. SCI. v. 21, p. 683-6, July 1960.

31. Tessler, J. and Fellowes, O.N.

The effect of gaseous ethylene oxide on dried foot-and-mouth disease virus. (Plum Island Animal Dis. Lab., Greenport, Long Island, N.Y.) AM. J. VET. RES. v. 22, p. 779-782, 1961.

Dried foot-and-mouth disease virus (FMDV) was inactivated under definite minimal conditions of relative humidity and temperature when exposed to the action of gaseous ethylene oxide (ETO) mixed with trichloromonofluoromethane (TMM) and dichlorodifluoromethane (DDM). After the FMDV was subjected to a 40% relative humidity (RH) for 30 minutes and then exposed to ETO at 90° or 78° F and 40% RH for 5 hours, the virus was inactivated as shown by tests in mice or tissue culture. Virus was not inactivated in 2 out of 3 trials after exposure to ETO for 5 hours at 40% RH and 98° F without prior humidification. The gases TMM and DDM did not inactivate the dried virus in the absence of ETO.

32. Thomas, J.A., et al
The chromatoclasic effect of ethylene oxide: Action on the purine and pyrimidine bases of nucleric acids. COMPT. REND. v. 251, p. 2797-9, 5 Dec 1960. (In French)

33. Thomas, J.A.
Method of bacteriological sterilization and disinfection without excess pressure by means of the controlled and brief synergic action of ethylene oxide and then of ozone. BULL. ACAD. NAT. MED. (PARIS) v. 144, p. 835-8, 20 Dec 1960. (In French)

34. Thon, D. and Neumann, M.
Experiences with sterilization by ethylene oxide. ZBL. BAKT. [ORIG.] v. 176, p. 256-9, Nov 1959. (In German)

35. Toth, L.Z.J.
Sterilizing effect of ethylene oxide vapor on different microorganisms. ARCH. MIKROBIOL. v. 32, p. 409-10, 1959.

36. Vango, S.P. and Krasinsky, J.B.
A METHOD FOR DETERMINING RELATIVE HUMIDITY IN STERILIZING GAS MIXTURE

36. (cont'd) CONTAINING ETHYLENE OXIDE, FREON 12, AND AIR. Jet Propulsion Lab., Calif. Inst. of Tech., Pasadena. Technical rept. no. 32-218, 1 Mar 1962, 19p. (Contract NAS 7-100) ASTIA AD-274 480.

A method for determining relative humidity in a sterilizing gas mixture containing ethylene oxide as the active ingredient was developed. The method entails the use of a commercially available instrument employing adiabatic cooling of the gas expanding rapidly from an observation chamber to obtain dew point temperatures.

37. Warner, P.

Recent advances in sterilization. Ethylene oxide.

CAN. HOSP. v. 38, p. 48-9 (Passim), Feb 1961.

38. Windmueller, H. G., et al

Reaction of ethylene oxide with nicotinamide and nicotinic acid. (Dept. of Biochem. and Nutr., Virginia Poly. Inst., Blacksburg, Va., USA)

J. BIOL. CHEM. v. 234, p. 889-894, 1959.

Ethylene oxide reacts with aqueous nicotinamide at 25° to give, after treatment with HCl, N^1 - (2-hydroxyethyl) nicotinamide chloride. This has no nicotinic acid activity for *Lactobacillus arabinosus* or for chicks, and it is not a nicotinic acid antagonist. Nicotinic acid is similarly converted into the betaine of N^1- (2-hydroxyethyl) nicotinic acid. The rate of reaction increases with increasing pH and temp. At higher pH values the products are unstable. The nicotinamide of DPN is unaffected. Under most conditions the acid is more reactive than the amide towards ethylene oxide. The bearing of the results on commercial ethylene oxide fumigation and other vitamin-ethylene oxide reactions is discussed.

39. Windmueller, H.G., Ackerman, C.J. and Engel, R.W. Reaction of ethylene oxide with histidine, methionine, and cysteine. (Dept. of Biochem. and Nutr., Virginia Poly. Inst., Blacksburg, Va., U.S.A.) J. BIOL. CHEM. v. 234, p. 895-899, 1959.

The decreased microbiological availability of histidine and methionine when proteins are treated with ethylene oxide appears to be due to hydroxy-ethylation of N and S atoms. Ethylene oxide reacts readily with histidine and imidazole in aq. soln. at room temperature to give the corresponding 1:3-bis- (2-hydroxyethyl) imidazolium deriv. With methionine or N-acethylmethionine, ethylene oxide hydroxyethylates the S to give the corresponding sulphonium derivative. Similarly the thiol group of cysteine is double-alkylated to give a sulphonium group. The primary amino groups of the amino acids are also alkylated, but the carboxyl groups are not attacked.