third ring component in griseofulvin is associated with a dramatic reduction of *in vitro* antidermatophytic activity.

Direct comparison of the fatty acid–griseofulvin derivatives (III*b*, IV*b*, V*b*) with the corresponding fatty acids (III*a*, IV*a*, V*a*) (Table III) indicated significantly enhanced antidermatophytic properties of the former entities in excess of the known and measured inhibitory properties of the individual fatty acids. However, none of the new compounds was as effective, on a microgram basis, as griseofulvin.

Several species differences could be demonstrated (Tables II and III). Compound I*b* (Table II), for example, was severely inhibitory for *T. mentagrophytes*, but was not at all effective against *M. gypseum* or *T. rubrum*. The single strain of *K. ajelloi* utilized in these experiments was quite resistant to amounts of griseofulvin which normally inhibit pathogenic dermatophytes (Table II). It was, however, inhibited by several of the griseofulvin derivatives at higher concentration. The isolate used was obtained from soil; it has been reported that soil isolates are relatively resistant to griseofulvin in contrast to pathogenic strains from clinical infections which tend to be griseofulvin sensitive (5). It may be added that definite species differences in the sensitivity to various compounds is of major interest in terms of the ultimate tailoring of a molecule for a specific effect.

The general concept of a skin-directed molecule also incorporating moieties for different therapeutic effects can, of course, be extended to several other situations such as those requiring antibacterial, antiyeast, and anti-inflammatory activities. Success from such an approach may well be based upon the synthesis of a graded series of derivatives such as those reported in this communication.

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Determination of 2-Chloroethanol in Surgical Materials by Extraction and Gas Chromatography

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Abstract □ A method for the determination of 2-chloroethanol in ethylene oxide sterilized surgical materials is described. The 2-chloroethanol is extracted under vacuum, condensed in a cold trap, and quantitative determinations made by GLC. The method is compared with acetone and water extractions.

Keyphrases □ Ethylene oxide sterilized plastic, rubber—2-chloroethanol determination □ 2-Chloroethanol extraction, determination—surgical materials □ GLC—analysis

Methods for the determination of 2-chloroethanol (ethylene chlorohydrin) in foods, plastic, and rubber have recently appeared in the literature (1–5). We have found these methods to be unreliable for this determination in polyvinyl chloride plastic (PVC), and in synthetic and latex rubber.

Cunliffe and Wesley (2) used saline and blood extraction to demonstrate the formation of 2-chloroethanol in solution by surgical plastics sterilized with ethylene oxide. None was found when distilled water was used. They did, however, find 2-chloroethanol in irradiated PVC which was subsequently sterilized with ethylene oxide. Irradiation formed HCl within the PVC which reacted with the ethylene oxide. This demonstrated that either absorbed ethylene oxide reacted with Cl^- within the plastic-forming 2-chloroethanol, or that the reaction took place in the elution liquid. The formation of 2-chloroethanol, due to Cl^- in PVC which had not been irradiated, was not demonstrated. It cannot be clearly shown by their method that 2-chloroethanol was formed during the sterilization process, but only that irradiation prior to ethylene oxide exposure resulted in the presence of detectable quantities of 2-chloroethanol in an elution solvent (*i.e.*, H_2O).

A method has been developed which appears to be reliable for determining 2-chloroethanol in a variety of materials. Extraction of 2-chloroethanol is achieved by heat and high vacuum distillation with collection in a U tube cooled in liquid nitrogen. The collected 2-chloroethanol was quantitatively determined by GLC. This method was compared with other reported techniques for determination of 2-chloroethanol.

EXPERIMENTAL

Apparatus—A 250-mlg. round-bottom flask with 24/40 ground-glass joint; glass tube with ground fitting for attachment to flask; fitting (Swagelock) to adapt glass tube to steel; stainless steel U tube, 0.305 m. length × 0.635 cm. o.d. (1 ft. length × 0.25 in. o.d.); vacuum source capable of less than forty μ. Gas chromatography was performed on an instrument (Perkin Elmer model 800) equipped with a dual-flame ionization detector. Also used was a column [0.318 cm. × 1.829 m. (1/8 in. × 6 ft.) ss 10% polyethylene glycol (Carbowax 1540) on Teflon 35M].

Table I—Recovery of 2-Chloroethanol

Material	mg. Absorbed	mg. Recovered	Recovery, %
PVC plastic	11.0	11.0	100
PVC plastic	10.5	10.5	100
Latex rubber	3.73	3.22	86.3
Latex rubber	1.7	1.49	87.7
Synthetic rubber	1.63	0.62	38.0

The operating parameters were: helium flow rate—29 ml./min.; 40 psig air zero gas (Matheson); 16.5 psig hydrogen; temperature of column: 125°; temperature of injection block: 200°; and temperature of detector: 195°.

Procedure—The plastic and rubber material tested were exposed in a commercial sterilizer to 750–800 mg./l. ethylene oxide for 4 hr. After sterilization, samples were cut, weighed, and placed in a round-bottom flask. Plastic tubing and other thicker material was first chilled in liquid N_2 and crushed to increase surface area. The flask was attached to the U collection tube *via* the glass tube and fitting. The U tube was immersed 2.54 cm. (1 in.) into liquid nitrogen in a Dewar flask. The U tube was then evacuated to at least 20 μ for 30 min. The flask was immersed in a water bath at 80–90° and evacuated 1 additional hr. After extraction, the vacuum was discontinued and the U tube allowed to warm to ambient temperature (20°). The content of the U tube was dissolved in a small amount of water (3–10 ml.) and transferred to a suitable container. Samples of 0.2 and 1.0 μl. were injected into the gas chromatograph.

2-chloroethanol elutes from the GC column in 5 min.; any ethylene oxide that is not volatized as the tube is warmed is separated from the 2-chloroethanol on the column and eluates in less than 1 min.; consequently there is no interference.

A standard calibration curve was prepared using 2-chloroethanol (Eastman Organic Chemicals) in water. Recovery studies to determine the efficiency of the method were performed by placing a small beaker containing 0.2 ml. of 2-chloroethanol in a 1,500-ml. container. Samples of the plastic or rubber material under investigation were placed in the container next to the beaker. The container was subsequently closed to create an atmosphere of 2-chloroethanol in the plastic or rubber environment. Exposure for 4 hr. at 20° was sufficient for the sample to sorb 10–20 mg. In the case where 100% recovery was achieved, the sample, after vacuum, returned to its original weight. In the determinations, where less than 100% recovery was achieved, and samples, after vacuum, did not return to their original weight. The increase could not be correlated with the 2-chloroethanol not recovered.

RESULTS AND DISCUSSION

Table I indicates the per cent recovery achieved with three materials used in determining efficiency of the method. Increased temperature of the water bath and vacuum for 3 hr. did not increase the amount recovered from the synthetic rubber. The 2-chloroethanol may have irreversibly reacted with the synthetic material. The same phenomenon to a lesser degree may be true in the case of latex. When water or acetone was tested as an eluting solvent, the percent recovery in each case was lower.

Table II—2-Chloroethanol Recovered from Sterilized Samples, mg./g.

Sample	Water Extraction	Acetone Extraction	Vacuum Extraction
A	0.207	0.188	0.323
B	0.112	0.048	0.142
C	NR[a]	NR	0.00059
D	NR	NR	0.00045

[a] NR = no recovery.

Table II lists results for three methods of extraction used for samples that were ethylene oxide sterilized. Samples A and B are polyvinyl chloride but of a different formulation. Sample C is synthetic rubber and Sample D is pure latex. A and B determinations were made immediately following sterilization. C and D were determined 14 days after sterilization.

Some formulations of polyvinyl chloride contain volatiles (plasticizers, extenders, *etc.*) which may have GC retention values equivalent to 2-chloroethanol and interfere with analysis. The control sample (unsterilized) will indicate this, if this is indeed the case. The frequency of this problem was not sufficient to warrant further work to separate the 2-chloroethanol from the volatiles. Of eight different formulations studied, only one contained interfering volatiles. For such difficult-to-analyze formulations, it would be necessary to evaluate other GC columns to effectively separate the 2-chloroethanol from the interfering volatiles.

The sensitivity of the instrument is 1 mcg./ml. using 0.2-μl. injections but by increasing sample size, detection limits are well below this value. Thus, values of 0.45 mcg./g. have been determined in latex. Other reported methods are limited by size of sample relative to extraction solvent volume, and would require an additional concentration step for the liquid extraction methods to acquire the same low-level sensitivity.

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