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# Detection of CL-912, a 1,3-Dioxalane, in Collapsible Tube Liner by Attenuated Total Reflection Spectroscopy

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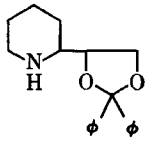
**Abstract** □ An attenuated total internal reflection technique was used to demonstrate the migration of the free base of CL-912C from a urological jelly to the lining of collapsible tubes during the sterilization cycle. This observation was substantiated by examination of isooctane extract of the sample liner by TLC and attenuated total internal reflection.

**Keyphrases** □ CL-912, a 1,3-dioxalane, in urological jelly—migration to collapsible tube liner, attenuated total internal reflection □ Attenuated total internal reflection—migration of CL-912 from urological jelly to collapsible tube lining □ Sterilization—migration of a 1,3-dioxalane from urological jelly to tube lining

Attenuated total internal reflection (ATR) has been established as a useful analytical tool. Briefly, the principles of ATR are as follows. When a beam of radiation enters a prism, it is reflected internally if the angle of incidence at the interface between the sample and prism is greater than the critical angle (Fig. 1). The internally reflected beam appears to penetrate slightly beyond the reflecting surface. If a sample that absorbs IR radiation is placed against the reflecting surface, the beam loses energy at those wavelengths where the sample absorbs.

A plot of intensity of reflected radiation as a function of wavelength resembles the absorption spectrum obtained by the transmission method. The apparent depth to which the radiation penetrates the sample is limited to a few microns and is dependent on the ratio of refractive indexes and the angle of incidence. Consequently, this technique has made possible the applications of IR spectroscopy in areas where it was not previously possible, such as with polymers, resins, leather, rubber, thin coatings, condensed GC fractions, fibers, and fabrics (1–3). Authentication of delicate objects like postage stamps have been carried out using ATR (4, 5); induced changes in biological tissues can also be detected (6). In this study, its usefulness in demonstrating the migration of (−)-2,2-diphenyl-4-(2-piperidyl)-1,3-dioxalane (CL-912) from a jelly to the lining of collapsible tubes is discussed.



CL-912

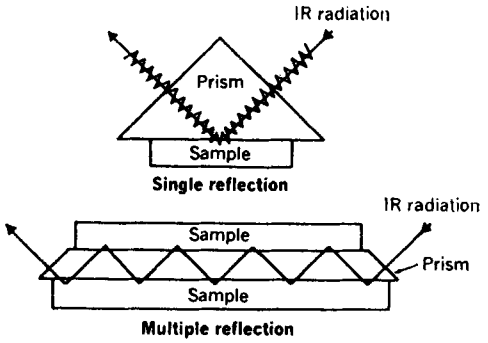


**Figure 1**—*Schematic diagram of single and multiple reflections.*

A prior-to-fill assay on urological jelly containing (−)-2,2-diphenyl-4-(2-piperidyl)-1,3-dioxolane hydrochloride (CL-912C)[1] indicated that the calculated amount of CL-912C was present in the formulation, but the assay immediately after sterilization of samples showed an 8–10% loss of the drug (7). Either the drug was degraded during the sterilization cycle or was bound to the liner. Hydrolysis of CL-912 gives benzophenone and 2-piperidyl-1,2-ethanediol, but no appreciable quantities of these were found in the jelly (7). The present studies were undertaken to determine if intact CL-912C, its free base (CL-912), or the degradation products are adsorbed on the linear surface.

## EXPERIMENTAL

**Materials**—In all experiments, CL-912C[2] was used. The free base (CL-912) was prepared by dissolving the hydrochloride in a quantity of distilled water, liberating it by addition of 5 *N* sodium hydroxide, and extracting with isooctane. The solvent was removed under reduced pressure.

[1] Levoxadrol hydrochloride, Cutter Laboratories, Berkeley, CA 94710
[2] Cutter Laboratories, Batch BL-16.

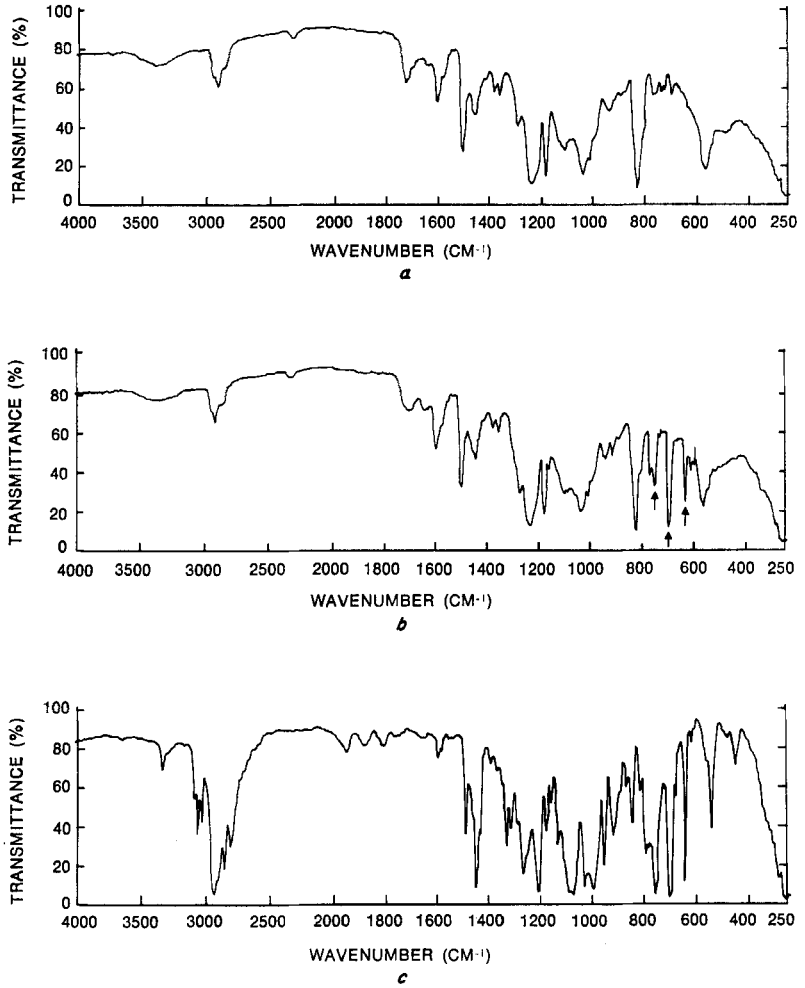



**Figure 2**—*ATR spectra of reference liner* (a), *sample liner* (b), *and CL-912* (c). *Arrows in Fig. 2b show major changes in the spectrum of sample liner due to migration of CL-912.*

A urological jelly containing 0.25% CL-912C in a water-soluble base of hydroxyethylcellulose[3] (1.85%), polyethylene glycol 400 (10.0%), sodium succinate (0.27%), and methylparaben (0.015%) was used. The jelly was filled in collapsible tin tubes lined with phenol–formaldehyde–epoxy resin and steam sterilized.

TLC was carried out on precoated silica gel plates without fluorescent indicator[4] using hexane. Iodine vapors were used to locate the spots.

**Equipment**—ATR spectra were recorded on a Perkin-Elmer IR grating spectrophotometer, model 457, using the Wilk's ATR accessory model 50 with a 45°-2 mm. KRS-5 plate and 45° angle of incidence.

**Procedure**—Empty tubes were used to obtain the spectrum of the unused liner (reference liner). Tubes containing CL-912C jelly were emptied, flushed well, and washed with distilled water. The tubes were cut open with scissors and blotted dry, and an ATR spectrum of the liner surface was obtained (sample liner).

## RESULTS

Comparison of the ATR spectra of reference and sample liners reveals an overall similarity, except in the 800–600-cm.$^{-1}$ region. The reference liner (Fig. 2*a*) shows weak bands in this region (765, 755, 725, 698, and 638 cm.$^{-1}$), whereas sample liners (Fig. 2*b*) show intense bands at 770, 755, 700, and 638 cm.$^{-1}$. In addition, change in contours of the bands at 1458, 1235, 1038, and 935 cm.$^{-1}$ are notable. An examination of an ATR spectrum of CL-912 (Fig. 2*c*) indicates that these differences are attributable to the adsorption of free base on the liner. In addition, isooctane extraction of the sample liners and removal of solvent afford an oil identified as CL-912 by comparing its ATR spectrum and TLC (single spot) with an authentic sample. Migration of CL-912 can be rationalized as follows. The jelly contains CL-912C, a salt of a weak base and strong acid in an aqueous buffered medium of pH 6.4. The pH of buffers can change markedly owing to significant changes in $K_w$ with temperature. Thus, the salt is subject to hydrolysis and capable of giving rise to the free base CL-912, which is preferentially adsorbed on the liner.

[3] Natrosol 250H, Hercules Powder Co., Wilmington, DE 19800
[4] Merck, Darmstadt, West Germany.

## SUMMARY

A comparison of ATR spectra of reference liner, sample liners, and CL-912 revealed the migration of free base to the liner. Awareness of such migration could lead to a more rational and scientific approach to selection of liners for collapsible tubes.

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