# THE STABILITY OF VINYL ETHER (VINETHENE) *

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THE chemical stability of an anesthetic agent is one of its most important properties. Manufacturers have spared no effort to protect the patient from impure anesthetic drugs. Precautions include printing an expiration date on containers for drugs that may deteriorate, in addition to recommendations that any unused portion be discarded twenty-four hours after the bottle is opened. Chemical experiments have been completed to show that the recommendations of the manufacturers of vinyl ether could be more liberal and still be adequate for protection.

Divinyl ether, $H-\underset{H}{C}=\underset{H}{C}-O-\underset{H}{C}=\underset{H}{C}-H$, is a symmetrical unsaturated organic oxide prepared from B–B′ dichlor-ethyl-ether and is less stable than its saturated counterpart, ethyl ether. Oxidation, heat, light, and acids hasten its deterioration to various aldehydes, organic oxides and acids, with subsequent polymerization of these compounds to resins (1). Since deterioration is retarded by alkaline substances, the product is marketed with .01 per cent. phenyl-alpha-naphthylamine which acts as an inhibitor of oxidation and imparts a purplish fluorescence to the liquid. With 3.5 to 4 per cent. absolute alcohol the mixture is marketed under the trade name of Vinethene. This product is packed in dark brown bottles with a hard rubber screw cap covered by a plastic film for tight sealing. A metal dropper cap is supplied to replace the hard rubber seal.

Fifty different specimens of Vinethene were opened, samples for analysis were removed, and the containers were resealed by screwing the caps in the ordinary manner. No other precautions for tight sealing were taken. The specimens were exposed to conditions which are encountered clinically, such as extremes of temperature and of humidity, bright and subdued light, and repeated opening and closing. These conditions, frequency of analysis, and results are summarized in Table 1.

Qualitative chemical tests that were completed were those outlined by the Council on Pharmacy and Chemistry of the American Medical Association (2) for determining the purity of the drug. Reducing substances (aldehydes) were detected with a solution of ammoniacal silver hydroxide and alkaline phloroglucinol. In addition to the recommended tests, oxidizing substances (peroxides) were detected by using a mix-

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TABLE 1

SAMPLES OF VINETHENE ANALYZED AND THE NUMBER AND TIME OF ANALYSES

No positive results were recorded

| Number of Specimens | Storage | | Examination |
|---|---|---|---|
| | Days | Conditions | |
| 6 | 10 | 10 cc. Half- | |
| 6 | 10 | 25 cc. filled | |
| 6 | 10 | 50 cc. bottles 26–32 C. | Daily |
| 6 | 7 | 10 cc. Full | |
| 6 | 7 | 25 cc. bottles | Alternate days |
| 6 | 7 | 50 cc. 26–32 C. | |
| 6 | 10 | 10 cc. Dark | |
| 6 | 10 | 25 cc. refrigerator | Alternate days |
| 6 | 10 | 50 cc. 4 C. | |
| 3 | 10 | 25 cc. Half-filled Low humidity | Alternate days |
| 3 | 10 | 25 cc. 26–32 C. 100% humidity | Alternate days |
| 3 | 10 | 25 cc. opened in 95% humidity | Tenth day |
| 3 | 10 | 25 cc. opened in 60% humidity | Tenth day |
| 2 | 5 | 25 cc. Half-filled light glass bottle | Daily |
| 3 | 3* | 25 cc. Half-filled 26–32 C. with dropper cap | Daily |
| 4 | 7 | 10 cc. Half-filled | |
| 4 | 7 | 25 cc. " " dropper cap 4 C. | Daily |
| 2 | 4 | 25 cc. Half-filled | |
| 2 | 4 | 50 cc. " " 26–32 C. dark room | Alternate days |
| 3 | 10 | 50 cc. 9 mos. outdated | Daily |

* Evaporated 3 days.

ture of sodium thiocyanate and ferrous sulphate, and acetylides with cuprous ammonium chloride reagent. Tests for odor and residue were also executed as recommended. In addition to the litmus test for acids, aqueous nitrazine was used to determine acidity or alkalinity.

Specimens that were opened and stored in an environment of 4 C. 26 to 32 C. with 100 per cent. relative humidity, and 26 to 32 C. in a dry atmosphere, showed no deterioration in ten days. Specimens opened in an environment of 60 per cent. and 95 per cent. humidity and then stored for ten days were free from deterioration. When stored at 4 C. for seven days and then removed to a warm environment for 48 hours, there was no deterioration. Deterioration was not influenced by the dropper cap, as compared with the ordinary cap, nor by subdued light, bright light, nor the absence of light. No difference was noted between partly empty and full bottles, nor between the small and large sizes. Specimens stored at low temperatures were not subject to evaporation, as were those stored at room temperature, particularly when not equipped with dropper caps. Vinyl ether boils at 28 to 31 C. and evaporates rapidly at room temperature.

Three samples which were kept in the original container were examined nine months beyond the expiration date and were found to be free from deterioration. These samples maintained this status for a ten day period. Eighteen specimens which were opened, examined, and sealed for seven days, and then reëxamined, were used for surgical anesthesia without unusual phenomena or reactions.

*Summary.*—Vinyl ether (Vinethene), once opened, may be sealed by replacing the cap, and the remaining portion may be used within a period of ten days without fear of deterioration. A cool storage place, free from chemical fumes, is preferred. Three samples examined suggest that the drug in the unopened container is stable for a period much longer than that represented by the expiration date on the bottle.

## REFERENCES

1. Ruigh, W. L., and Major, R. T.: Preparation and Properties of Pure Divinyl Ether, J. Am. Chem. Soc. 53: 2662 (July) 1931.
2. New and Nonofficial Remedies, American Medical Association, 1938, p. 55.

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At the meeting of the Council on Medical Education and Hospitals held in Chicago on February 16, 1941, that body unanimously approved the motion that the American Board of Anesthesiology, Inc., be made a Major Board, thus severing its affiliation with the American Board of Surgery. This action was taken following the approval of seven boards, namely, The American Boards of Ophthalmology, Otolaryngology, Obstetrics and Gynecology, Orthopedic Surgery, Surgery, Urology, and Anesthesiology.