Idoxuridine—A Preliminary Report

By LOUIS J. RAVIN, CHARLES A. SIMPSON, and ALFRED F. ZAPPALA

Data are presented to show that the principal decomposition products of idoxuridine ophthalmic solution in acidic media (pH 1.3 to 6.7) are 5-iodouracil and 2-deoxyribose. A trace of 2′-deoxyuridine was also detected. Uracil was not formed under the conditions of these experiments.

During the development of a clinically acceptable idoxuridine ophthalmic solution it was necessary to determine the type of breakdown products formed during storage at temperatures ranging from 5 to 60°. This note presents some preliminary information concerning the nature of the decomposition products formed when idoxuridine ophthalmic solution is artificially decomposed in acidic media (pH 1.3 to 6.7).

A column partition chromatographic procedure was developed (1) and subsequently used to separate the decomposition products from the idoxuridine. The individual components were then assayed by spectrophotometric methods.

Idoxuridine, some possible decomposition products, and an artificially decomposed solution of idoxuridine ophthalmic solution were chromatographed on paper using a *n*-butanol–3 *N* ammonia solvent system. A comparison of the approximate R_f values obtained are listed in Table I.

It can be seen from these data that the principal products formed when idoxuridine ophthalmic solution decomposes in acidic solution are 5-iodouracil, 2-deoxyribose, and 2′-deoxyuridine. Subsequent analysis of degraded samples by the partition column procedure substantiated that the breakdown products formed under these conditions are 5-iodouracil, 2-deoxyribose, and a trace of 2′-deoxyuridine. Figure 1 shows a plot of per cent idoxuridine *versus* per cent 5-iodouracil. The linear relationship having a slope of 0.95 indicates that for every mole of idoxuridine that decomposes, approximately 1 mole of 5-iodouracil is formed, further indicating that 5-iodouracil and 2-deoxyribose are the principal breakdown products. Uracil was not detected in the decomposed samples under the conditions of this study.

Received June 13, 1963, from the Research and Development Division, Smith Kline and French Laboratories, Philadelphia, Pa.
Accepted for publication October 14, 1963.

Table I.—Comparison of Approximate R_f Values Obtained for Idoxuridine, Some Possible Decomposition Products, and An Artificially Decomposed Ophthalmic Solution

Material	R_f Values: Known Soln.	R_f Values: Artificially Decomposed Soln.
2′-Deoxyuridine	0.23	0.23 (Trace)
Uracil	0.28	...
Idoxuridine	0.31	0.31 (Large)
2-Deoxyribose	0.37	0.39 (Significant)
5-Iodouracil	0.50	0.48 (Significant)

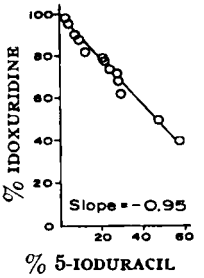

Fig. 1.—Plot showing decreasing idoxuridine and increasing 5-iodouracil concentrations for artificially decomposed idoxuridine ophthalmic solutions.

REFERENCE

(1) Smith Kline and French Laboratories, to be published.

Thin-Layer Chromatography of Iodochlorhydroxyquin

By B. P. KORZUN, S. M. BRODY, and F. TISHLER

A thin-layer chromatographic method is described for the separation of iodochlorhydroxyquin and its intermediates. The method is applicable not only to the substance but also to its pharmaceutical formulations, in which the material is suspended in ointment or cream.

The present analytical procedures (1–4) available for determining iodochlorhydroxyquin,[1] both as the substance and in formulations, do not distinguish between iodochlorhydroxyquin and its possible intermediates. The colorimetric procedure of Haskins and Luttermoser (2) and the paper chromatographic procedure of Castiglioni (3), although capable of separating 8-hydroxyquinoline from iodochlorhydroxyquin, do not separate iodochlorhydroxyquin from other halogenated hydroxyquinoline intermediates.

A semiquantitative thin-layer chromatographic procedure, using polyamide as the adsorbant, has been developed which separates iodochlorhydroxyquin from all probable intermediates, except 5,7-dichlorohydroxyquinoline. In combination with iodochlorhydroxyquin, the limit of detection is 0.25 mcg.

Received October 18, 1963, from the Research Department, Ciba Pharmaceutical Company, Division of Ciba Corporation, Summit, N. J.
Accepted for publication November 12, 1963.
[1] Marketed as Vioform by Ciba Pharmaceutical Co., Summit, N. J.