Induction of Intestinal Tumours by N-Ethyl-N-nitrosourethane

INTESTINAL tumours, though very rare in laboratory rodents, have been induced by several types of carcinogenic agents, including polycyclic aromatic hydrocarbons, 4-dimethylaminostilbene, 2-acetyl-aminofluorene and radiation[1,2]. However, so far, no such tumours have been induced by alkylnitroso-compounds, which are able to induce tumours in many organs[3]. Attempts to induce tumours of the colon by repeated rectal application of diethylnitrosamine led to liver, but not to local, tumours[4].

It is of interest, therefore, that when *N*-ethyl-*N*-nitrosourethane (ENU) in 50 per cent aqueous ethanol was given to rats, males and females, by intraperitoneal injections, 3 out of 6 rats which survived more than a year developed adenoma and adenocarcinoma of the mucosa of the ileum. The tumours were multiple and were found in two male and one female rat, killed 16·5, 20 and 18 months after the first and 6, 9·5 and 7·5 months, respectively, after the last of four doses of ENU, about 20 mg per rat, *in toto*. The tumours formed large cauliflower-type nodules, up to 1·5 cm diameter, obstructing the lumen, and caused enormous distension of this part of the intestine. Some of the nodules penetrated into the muscle layer of the intestinal wall. *N*-Methyl-*N*-nitrosourethane, the methyl-homologue, is only now being tested by the intraperitoneal route in rodents.

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1 Fischer, W., and Kühn, I., *Geschwülste der Laboratoriumsnagetiere* (T. Steinkopff, Dresden, 1958).
2 Schoental, R., and Bensted, J. P. M., *Brit. J. Cancer*, **17**, 242 (1963).
3 Magee, P. N., and Schoental, R., *Brit. Med. Bull.*, **20**, 102 (1964).
4 Schmähl, D., Thomas, C., and König, K., *Z. Krebsforsch.*, **65**, 529 (1963).

BIOLOGY

Influence of Hexadecane on Absorption of Carbon Dioxide by Plants

RESULTS of recent investigations concerning the influence of hydrocarbons and a petroleum oil on apparent photosynthesis in *Citrus sinensis*[1] and *Bauhinia blakeana*[2] have focused my attention on the significance of stomatal distribution in a plant's response to the application of hydrocarbons. For example, using infra-red carbon dioxide analysis with sequential multi-point sampling[3], it has been shown that an application of a paraffinic hydrocarbon to either the upper or lower surface of the leaves of *Bauhinia blakeana* results in a decrease of absorption of carbon dioxide while a similar application to the leaves of *Citrus sinensis* results in a decrease of absorption of carbon dioxide only when applied to the lower surface of the leaves. Since these results are corollary to the distribution of stomata in these species they suggest penetration only through stomata with consequential interference of absorption. The present investigation was initiated in order to clarify further the role of stomatal distribution.

With the following exceptions, infra-red carbon dioxide analysis as previously described[3] was used. Leaves of *Heliconia humilis* were enclosed in water-cooled plastic chambers which permitted sequential sampling for 5-min periods from either the lower or upper surfaces. The leaves were sufficiently illuminated from above to obtain maximum apparent photosynthesis (carbon dioxide absorption) from both surfaces. After a pattern of carbon dioxide absorption was established for both surfaces, applications of hexadecane were made using a settling tower loaded from an aerosol container. The amounts of hexadecane were determined gravimetrically.

The result of an initial application of 79 μg/cm² on the upper surface is shown in Fig. 1*a*, while the result of an initial application of 126 μg/cm² on the lower surface is shown in Fig. 1*b*. For clarification the dark periods (respiration or carbon dioxide evolution) have been omitted. Corrections have been made for minor fluctuations of carbon dioxide in air.

Initially, and as anticipated from the distribution of stomata in this species, approximately 20 times as many on the lower surface as on the upper, a greater amount of carbon dioxide is removed from the air stream passing over the lower surface[4]. With the application of hexadecane to either surface a depression of carbon dioxide absorption is obtained. It should be noted that the application to the upper surface did not interfere with absorption from the lower surface; and, conversely, the application to the lower surface did not interfere with absorption from the upper surface. These results suggest the lack of complete hydrocarbon penetration at the levels used.

Recovery from the application appears to correlate with the dissipation of the hydrocarbon. Complete recovery from the application applied to the lower surface occurred in about 6 h, while complete recovery from the application to the upper surface was not apparent until after stomatal opening the following morning. The variance between the time of complete evaporation of the hydrocarbon from the aluminium paper strips and complete recovery of carbon dioxide absorption can undoubtedly be attributed to the 'threshold levels' that result from sorption.

The results unequivocally demonstrate the significance of stomatal distribution in a plant's response to the

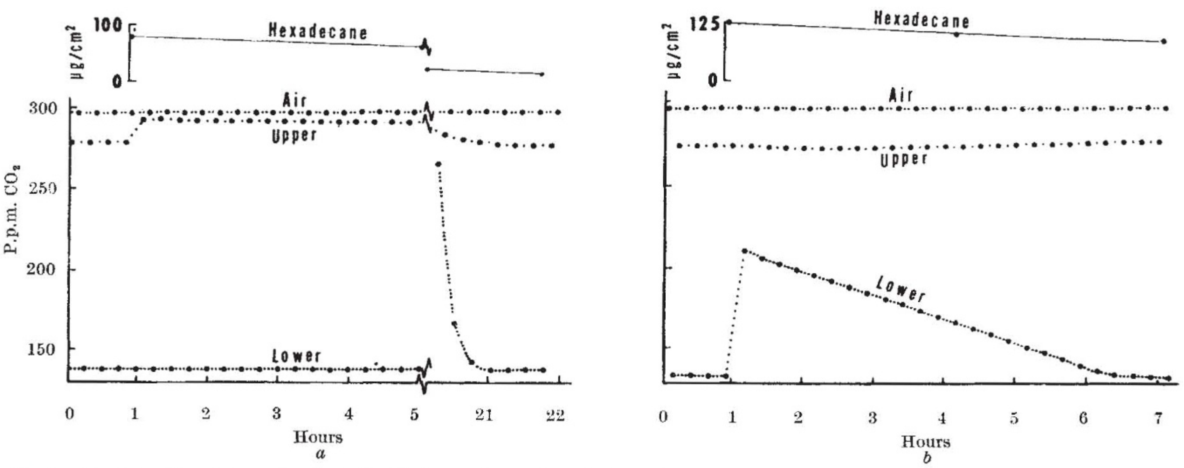

Fig. 1. Concentration, p.p.m. of carbon dioxide in air stream from 3 channels sampled sequentially. Each large dot represents one 5-min sampling period. Solid line represents evaporation of hexadecane from aluminium paper strips, μg/cm². *a*, Application to upper surface; *b*, application to lower surface. Dark periods not shown