Variations in the Inhibitory Power of Carcinogenic Hydrocarbons according to the Solvent

PEACOCK[1] has noted a difference in the carcinogenic power of certain hydrocarbons injected subcutaneously, according to the solvent used. This potency reaches its maximum in the case of lard or olive oil, and its minimum with fats obtained from the same species.

We judged it useful to find whether by varying the solvent any difference would be produced in the inhibitory action, possessed by carcinogenic compounds[2], on the growth of transplantable tumours. In the first tests, made on rat tumours, we used as solvent a fat obtained from this species by successive extractions with acetone, hot and cold alcohol and ether. In the final ether solution, small quantities of undissolved substances were filtered off. The action of the hydrocarbon dissolved in this lipoidal mixture was compared with that of the same substance dissolved in lard, or in colloidal suspension. In a first series of tests, rats in which Walker carcinoma had been grafted 4 days earlier were subdivided as follows: (*a*) 14 control rats injected twice with 1 c.c. of untreated lard with an interval of one week; (*b*) 14 rats injected twice with 3 mgm. of 3 : 4-benzpyrene dissolved in 1 c.c. of rat fat, with an interval of one week; (*c*) 14 rats injected twice with the same quantity of hydrocarbon dissolved in 1 c.c. of lard, with an interval of one week.

In a second series of tests, rats bearing Walker carcinoma were treated as follows: (*a*) 12 control rats injected twice with 2 c.c. of untreated lard, with an interval of one week; (*b*) 12 rats injected twice with 3 mgm. of 1 : 2 : 5 : 6-dibenzanthracene dissolved in 2 c.c. of rat fat, with an interval of one week; (*c*) 12 rats injected twice with the same quantity of hydrocarbon dissolved in 2 c.c. of lard, with an interval of one week.

Lastly, in a third series, we have compared the inhibitory power of 3 : 4-benzpyrene dissolved in lard and injected subcutaneously with that of the same substance administered in colloidal suspension by intravenous injection (30 rats for each test).

The results proved that the highest inhibitory power was obtained by subcutaneous injection of the hydrocarbons in lard. The colloidal solution given intravenously showed a less constant activity. *In mixtures of homologous lipoids and fats* (that is, fats obtained by extraction from rats and injected into animals of the same species) *there is a total suppression of the inhibitory power for* 3 : 4-*benzpyrene and a distinct diminution for* 1 : 2 : 5 : 6-*dibenzanthracene.*

This last fact cannot be easily ascribed to a more rapid elimination of the compound due to easier absorption of the solvent. In fact, when the animals died on account of the tumour, autopsy showed that most of the fat remained at the site of injection, where it determines a more rapid and more intense inflammatory reaction than is the case with lard. A formation of ulcers earlier than in the case of lard was also observed (10–15 days).

Tests are being carried out to explain this anomalous behaviour of homologous fat as a solvent of the carcinogenic hydrocarbons.

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E. MORELLI.
A. DANSI.

[1] Peacock, *Proc. Leeuwenhoek-Vereeniging* 1935. See also Beck, *Brit. J. Exp. Path.*, **19**, 31 (1938).

[2] Haddow, NATURE, **135**, 868 (1935). Morelli, *Boll. lega It. per la lotta contro il Cancro*, 1936. Morelli and Dansi, *Second Internat. Cancer Congress*, Brussels, **2** (1936). Haddow, *ibid.*

Permeability of Corpuscles and Muscle Cells to Potassium Ions

AN almost ideal method to study the permeability of corpuscles is to introduce into the plasma cations, for example, ions of potassium labelled by the addition of a radioactive potassium isotope, to separate after the lapse of a certain time the corpuscles, and to determine if and to what extent the latter contain radioactive potassium ions.

^{42}K, which has a half-life time of 12 hours, was administered in the form of potassium chloride to a rabbit by subcutaneous injection. The active potassium was kindly prepared by Dr. J. C. Jacobsen and Mr. N. Lassen by means of the cyclotron in Prof. Bohr's institute. Blood samples were taken at intervals, the corpuscles were separated from the plasma by centrifuging, washed twice with inactive plasma and the activity of both the corpuscles and the plasma determined. After the lapse of twenty-four hours the animal was killed, and the activity of the different organs was also determined.

As seen in the accompanying table, a part of the labelled potassium resorbed into the plasma is present in the corpuscles; but, even after the lapse of twenty-four hours, the activity of 1 gm. corpuscles amounts only to 66 per cent of that of 1 gm. plasma. As 1 gm. corpuscles contains about twenty times more potassium than 1 gm. plasma, the above figure has to be divided by 20 to arrive at the figure representing the extent of equipartition of the individual potassium ions present in the plasma at the start of the experiment between the plasma and the corpuscles.

Thus, 3 per cent of all individual potassium ions present in the aggregate of the corpuscles at the end of the experiment were incorporated in the course of the last 24 hours. A part of this 3 per cent is due to the formation of new corpuscles, since corpuscles formed in an organism containing labelled potassium must certainly contain labelled potassium; furthermore, some of the ^{42}K ions found in the corpuscle fractions may have been adsorbed on the surface, some may be penetrated into the corpuscles. From the above figures it follows that the permeability of corpuscles to potassium ions is certainly very minute, or more correctly, the bulk of the potassium ions present in the corpuscles is not replaced within the life-time of the latter. Incidentally, we can conclude that the formation of new corpuscles within twenty-four hours is restricted to 3 per cent of the total corpuscle content of the rabbit.

DISTRIBUTION OF ^{42}K.

Time	Organ	Percentage of ^{42}K administered present in 1 gm. fresh substance*
16 min.	Plasma	$2{\cdot}0 \times 10^{-2}$
35 ,,	,,	$2{\cdot}4 \times 10^{-2}$
61 ,,	,,	$2{\cdot}7 \times 10^{-2}$
93 ,,	,,	$3{\cdot}3 \times 10^{-2}$
3 hours	,,	$3{\cdot}0 \times 10^{-2}$
7 ,,	,,	$3{\cdot}0 \times 10^{-2}$
15·5 ,,	,,	$3{\cdot}0 \times 10^{-2}$
19·5 ,,	,,	$3{\cdot}1 \times 10^{-2}$
24·5 ,,	,,	$2{\cdot}9 \times 10^{-2}$
24·5 hours	Corpuscles	$1{\cdot}9 \times 10^{-2}$
24·5 ,,	Muscles	$4{\cdot}2 \times 10^{-2}$
24·5 ,,	Liver	$4{\cdot}1 \times 10^{-2}$
24·5 ,,	Kidneys	$4{\cdot}7 \times 10^{-2}$
24·5 ,,	Brain	$2{\cdot}8 \times 10^{-2}$
24·5 ,,	Tibia epiphysis	$3{\cdot}1 \times 10^{-2}$
24·5 ,,	Tibia diaphysis	$1{\cdot}9 \times 10^{-2}$
24·5 ,,	Marrow	$2{\cdot}3 \times 10^{-2}$
24·5 ,,	Spleen	$3{\cdot}3 \times 10^{-2}$

* When evaluating the above figures due regard was taken of the activity of the tissue potassium due to ^{40}K.