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THE ONCOGENIC EFFECTS OF VINYL CHLORIDE ADMINISTERED BY ORAL ROUTE IN THE RAT

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IN THE FIELD OF RESEARCH

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SECOND PRELIMINARY NOTE

As has already been reported, a vast program of experimental research was initiated at our institution to define the oncogenic activity of vinyl chloride (VC) administered by different routes (inhalation, oral, subcutaneous, intraperitoneal) at different doses, to animals of various species (rats, mice, hamsters) and different strains. From these experiments it has become apparent that vinyl chloride, when administered by inhalation, provokes various types of tumors in different animal species: in the rat, carcinomas of the Zymbal glands, nephroblastomas, angiosarcomas and angiomas of the liver and of other anatomical regions, cutaneous carcinomas, hepatomas, neuroblastomas, mammary carcinomas and probably carcinomas of the salivary glands; in the mouse, pulmonary adenomas (frequently in the stage of malignant transformation), mammary carcinomas (often with acantotic components), angiosarcomas and angiomas of the liver and of other anatomical regions, cutaneous epithelial tumors; in the hamster, angiosarcomas and angiomas of the liver,

trichoepitheliomas and cutaneous basalomas, melanomas, papillomas and acanthomas of the fore-stomach, hepatomas and probably lymphomas (Maltoni, 1975; Maltoni and Lefemine, 1974 a, b: Maltoni and coll., 1974: Maltoni and Lefemine, 1975). Recently we have observed a significant incidence of papillomas and acanthomas of the fore-stomach in rats treated with vinyl chloride by inhalation at the rate of 50,000 ppm (unpublished data).

It was following the first announcement of our results that the clinical observations got underway and the epidemiological investigations that have led to the finding of occupational angiosarcomas in working populations exposed to the monomer and, in the same populations, a higher incidence of encephalic neoplasia, pulmonary carcinoma, lymphoma and leukemia.

On February 22, 1975, we made known the very first results of our experiment BT 11 on the oncogenic activity of vinyl chloride administered by oral route: 50 weeks after the beginning of the experiment, an angiosarcoma of the thymus and a hepatic angiosarcoma were observed respectively in the two groups of rats treated with the highest doses — that is, 50 mg/kg of body weight and 16.65 mg/kg of body weight — 4 to 5 times a week for 50 weeks (Maltoni and coll., 1975).

Since polyvinyl chloride and other plastics in which vinyl chloride is a constituent are used as containers for liquid and solid food materials, and since traces of the monomer may migrate from the plastic to drinks and foods, the possible carcinogenic effect of

vinyl chloride by oral route takes on obvious importance for public health.

Since the studies on the oncogenic activity of vinyl chloride by oral route were first undertaken in our Institute and the only results on the subject are the very preliminary ones communicated by us this past February, we receive requests for information periodically from investigators who are responsible for the health of various countries, institutions and entities and who want to be brought up to date on the development of this experiment of ours.

In consideration of this, with this second preliminary note we are making public the results after 85 weeks of experimentation.

In experiment BT 11; on which we are reporting again here, the VC was administered to Sprague-Dawley rats 15 weeks old, dissolved in olive oil, by means of a gastric tube, 4—5 times a week for 52 weeks.

The experiment involved four groups of 80 animals each, treated with an equal volume of oil solution of vinyl chloride at various concentrations (20/1000, 6.60/1000, and 1.32/1000 respectively) so as to treat with 50 mg, 16.65 mg and 3.33 mg/kg of the animals' body weight, and with olive oil alone.

To adjust the quantity of vinyl chloride to the weight increase of the animals, the volume of solution administered was increased, varying from 0.42 cc to 1.12 cc.

The plan of the experiments and the 85-week results are shown in Table 1. From the results given there it can be seen that vinyl chloride administered by oral route at 50 mg and at 16.65 mg/kg of body weight is carcinogenic and provokes a large part of the tumors observed in the same species and strain when the monomer is administered by inhalation, although they are predominantly hepatic angiosarcomas. None of these tumors have been observed to date in the animals treated with vinyl chloride at doses of 3.33mg/kg of body weight nor in the controls treated with olive oil alone.

Since the doses used by us are very high in comparison with those that might migrate into foodstuffs from containers made of plastic materials based on vinyl chloride, we have undertaken another experiment, BT 27, since first finding tumors in experiment BT 11, in order to test the monomer at lower doses. The plan of these experiments is reproduced in Table 2.

Table 1

Experiment BT 11: Treatment: administration by oral route (gastric catheter) of vinyl chloride in olive oil at doses of 50.00, 16.65, 3.33 mg/kg of body weight once a day for four to five days a week for 52 weeks. Results after 85 weeks.

Groups and treatments	Animals (Sprague-Dawley rats) Totals	Survived	Animals with tumors: Carcinomas of glands of Zymbal N.	Nephroblastomas N.	Angiosarcomas Liver N.	Angiosarcomas Other Locations N.	Other types and/or locations (b) N.	Total N.
I VC 50.00mg/kg	80	23	—	—	8	1 (a)	3 (c)	11 (d)
II VC 16.65mg/kg	80	32	1	1	5	—	—	7
III VC 3.33mg/kg	80	39	—	—	—	—	—	—
IV Olive oil (control)	80	35	—	—	—	—	—	—
Total	320	129	1	1	13	1	3	18

a) 1 angiosarcoma of the thymus.

b) Various cases of mammary, fibroadenoma and tumors (generally adenomas) of the adrenals and of the hypophysis were not taken into consideration because their distribution in the different groups did not vary.

c) 1 mammary carcinoma; 2 papillomas of the pre-stomach.

d) 1 animal with 2 tumors.

Table 2

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Experiment BT 27: Treatment: administration by oral route (gastric catheter) of vinyl chloride in olive oil at doses of 1, 0.3 and 0.03 mg/kg of body weight once a day for four to five days a week for 104 weeks. Results after 22 weeks.

Groups and treatments	Animals (Sprague-Dawley rats) Totals	Survived	Animals with tumors					
			Carcinomas of glands of Zymbal	Nephro-blas-tomas	Angiosarcomas Liver	Angiosarcomas Other Loca-tions	Other types and/or loca-tions	Total
			N.	N.	N.	N.	N.	N.
I VC 1 mg/kg	158	147	—	—	—	—	—	—
II VC 0.3 mg/kg	159	143	—	—	—	—	—	—
III VC 0.03 mg/kg	163	147	—	—	—	—	—	—
IV Olive oil (control)	159	148	—	—	—	—	—	—
Total	639	585	—	—	—	—	—	—

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