ONCOLOGY

The Pharmacokinetics of (^{125}I)3-Deoxy-3-Iodine Glucose on Experimental Tumor Models *in Vivo*

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The dynamics of ^{125}I distribution is studied in rats with induced tumors of the prostate and mammary gland for intravenous administration of ^{125}I-3D-G. It is found that 80% of the activity is eliminated in the first 24 hours. A relatively high level of ^{125}I accumulation is found in necrotically altered regions of the tumor.

Key Words: *(^{125}I)3-deoxy-3-iodine glucose; rats; induced tumors; pharmacokinetics*

Radioactively labeled antibodies and some metabolites have recently attracted the attention of experimental and clinical oncologists as likely candidates for systemic radiotherapy [3,4,8]. One of the most fruitful groups of metabolites is the group of modified carbohydrates, although only 2D-^{18}F-glucose has been studied in depth, and then only as a carrier of the diagnostic label (^{18}F) [5,6]. Other representatives of the modified carbohydrate class have hardly been studied as potential carriers of therapeutic activity .

The present investigation was undertaken to determine *in vivo* the pharmacokinetic characteristics of (^{125}I)3-deoxy-3-iodine glucose (^{125}I-3D-G), one of the representatives of this group of metabolites.

MATERIALS AND METHODS

The study was performed with ^{125}I-3D-G synthesized at the Zelinskii All-Russian Research Institute of Organic Chemistry, Russian Academy of Sciences. The stability was checked by NMR-spectroscopy. Incorporation of the radioactive label in the preparation was performed by reiodination after Stevens [7], replacing stable I with ^{125}I. In the finished preparation the correlation of stable and substituted radioactive iodine was 20:1. Wistar rats (All-Russian Oncologic Research Center, Russian Academy of Medical Sciences) with induced malignant tumors of the mammary gland [1] and prostate [2] were used as a tumor model. The working solution of the preparation, prepared using saline, was administered under ether anesthesia in the femoral vein for 1 min at 1 ml volume and 5.8 kBq of activity. Rats were sacrified by an overdose of anesthesia. Tissue samples were immediately weighed and placed on paper filters in measuring cups of a radiometer. Drying of the samples was performed in dry heat at 80°C. Radiometry of the preparation and tissue samples was performed using an LB5100E alpha-beta-gamma radiometer (Tennelec) combined with a spectrophotometric plate (Nucleus). The measurement of samples of each series was performed 5 times in the automatic regime with an exposure of 1 min for each sample. The activity of a sample and the standard

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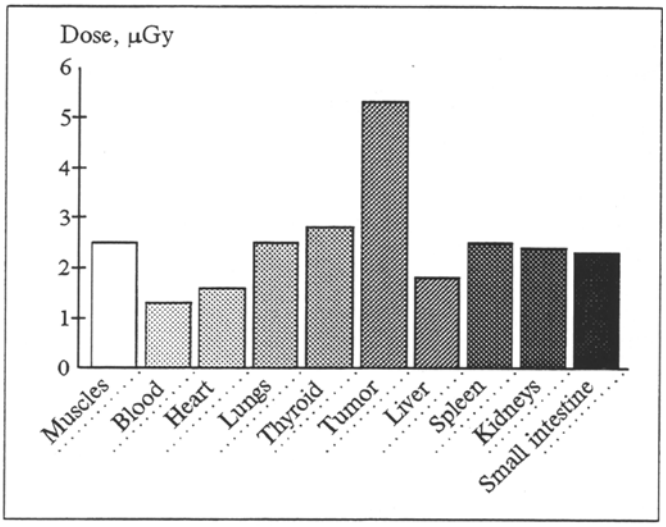

Fig. 1. Total absorbed dose in organs and tissues of tumor-bearing rats over 7 days in terms of ^{131}I radioactive label for i.v. administration of 1 ml $^{125}I-3D-G$ with a total activity of 5.8 kBq.

deviation of activity were calculated according to calibration coefficients obtained previously.

RESULTS

Data on the dynamics of the ^{125}I-3D-G concentration in different organs and tissues are listed in Table 1; 80% of the administered activity was eliminated from the organism after 1 day and the residual level of radioactivity in the tumor was 1.5-fold higher than the level of radioactivity in healthy tissues.

By the end of the 7th day the ratio of ^{125}I concentrations in the tumor and healthy tissues was 2-15. The preparation does not cross the blood-brain barrier and practically does not accumulate in the brain. The level of ^{125}I in the thyroid gland changed insignificantly during the whole period of the study and did not exceed 0.05% of the administered activity, which testifies to a sufficient resistance of the iodine bond with the glucose residue *in vivo*.

The total absorbed dose was calculated in different organs and tissues of tumor-bearing rats over 7 days when ^{131}I was used as a radioactive label (Fig. 1). The calculated level of the dose in the tumor was 2-4-fold higher than the dose in normal organs and tissues.

It is to be noted that the distribution of radioactivity in the tumors was characterized by nonuniformity with the maximal ^{125}I concentrations often found in zones of necrotic changes.

Thus, the intravenous administration of ^{125}I-3D-G to tumor-bearing rats results in the predominant accumulation of radioactivity in the tumor tissue. At the same time the total level of activity in the tumor (over 7 days) accounted for only 0.1% of the administered radioactivity. The value of the absorbed dose gradient, calculated according to ^{131}I, between the tumor and healthy tissue was 3.2 on average.

The indicated value is insufficient for systemic therapy using ^{125}I-3D-G. Nevertheless, the observed cases of high concentrations of radioactive label, in particular in the region of tumor necrosis, call for further study of the preparation *in vivo* using different tumor models.

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TABLE 1. Variation of ^{125}I Concentration (Bq/q Tissue) in Normal and Tumor Rat Tissue 1-7 Days after Intravenous Administration of $^{125}I-3D-G$

Organ	Time					
	30 min	2 h	day 1	day 2	day 4	day 7
Muscles	7.8±2.2	18.8±7.4	3.7±0.9	1.9±0.8	0.87±0.7	0.37±0.3
Blood	17.5±4.9	11.3±5.2	1.8±0.3	1.1±0.8	0.26±0.2	0.25±0.2
Heart	18.1±0.3	9.3±5.0	3.8±1.4	1.8±0.8	0.10±0.1	0.20±0.2
Lungs	15.8±0.4	7.9±5.1	3.3±0.8	1.8±1.2	2.00±1.9	1.80±0.3
Liver	17.3±0.1	12.4±3.5	1.6±0.8	1.1±0.3	0.43±0.4	1.80±1.5
Spleen	19.3±5.4	16.6±4.3	5.4±4.1	1.7±0.8	1.30±0.6	0.55±0.4
Kidneys	32.8±21.0	20.3±9.8	1.9±1.3	0.6±0.4	0.86±0.2	1.90±0.9
Small intestine	26.3±4.5	13.9±0.1	2.2±1.2	2.5±1.9	1.60±1.4	0.24±0.2
Thyroid	2.3±1.8	4.4±2.1	2.4±1.9	2.7±0.7	3.42±1.5	2.5±1.9
Tumor	24.9±1.3	15.7±6.1	7.8±3.1	4.3±1.9	3.11±1.0	5.75±1.5

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Time Course of the Binding of Some Prostanoids in the Serum of Mice with Lewis Lung Carcinoma with Spontaneous Metastases. Effect of Exogenous Prostaglandins on Tumor Dissemination

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It is shown that the ability of serum to bind some prostanoids changes depending on the stage of development of the primary tumor node. Surgical removal of the tumor modulates the binding of TxB_2. When the PGE_2 content increases in the organism, the PGE_2 binding in the serum is stepped up, and dissemination is enhanced.

Key Words: *Lewis lung carcinoma; metastasis; prostaglandins*

Prostaglandins (PG) are involved in the primary and secondary neoplastic processes [6], but the specific mechanisms of their action are not always clear.

The aim of the present study was to investigate the effect of prostaglandins E_2 and $F_{2\alpha}$ on the growth and spontaneous dissemination of Lewis lung carcinoma (LLC), as well as the organism's competence with respect to these prostanoids and TxB_2.

MATERIALS AND METHODS

The experiments were carried out on C57Bl/6 and BDF_1 mice of both sexes, with an initial weight of 19-23 g. Transplantation of tumor material from LLC was performed subcutaneously or intramuscularly by the routine method [3]. The primary tumor node was surgically removed on day 8 after transplantation. The mice were killed (diethyl ether) on days 21-25 of tumor carriership. After the mice had been killed, the weight of the primary tumor was recorded and the lungs were excised, divided into lobes, and placed in Bouin's fluid (time of exposure not less than 24 h). After fixation, the number of surface metastatic nodes was counted using an MBS-9 microscope (8×2). The rate of metastasis was assessed in terms of its incidence (the number of animals with metastases in % of the total number of mice in the group) and its severity (the mean number of metastatic nodes per mouse). The index of metastasis inhibition (IMI) was calculated by the formula:

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