

# ACTION OF EPIDERMAL CHALONES ON DEVELOPMENT AND GROWTH OF CHEEK

## POUCH TUMORS IN HAMSTERS

P. G. Godorozha, M. A. Zabezhinskii,  
V. B. Okulov, Yu. G. Puchkov,  
G. B. Pliss, and V. A. Aleksandrov

UDC 616-006-092.9-085.363.6.018+615.362.6-  
018.017.615.277.3

KEY WORDS: hamster; cheek pouch; tumors; chalones; antitumor action.

A promising trend in the search for antitumor agents is the use of tissue-specific inhibitors of proliferation (chalones). Experiments have demonstrated the inhibitory action of chalones on the tumor process [2, 6]. In particular, epidermal chalones (EC) delayed the development of squamous-cell tumors of the vagina and lower lip [1, 3].

The object of this investigation was to study the action of EC on development and growth of epithelial tumors of the hamster cheek pouch (CP), induced by a chemical carcinogen, namely 7,12-dimethylbenz(a)anthracene (DMBA). The neoplasms thus produced constitute an adequate model of human tumors of the oral cavity and they have frequently been used to study the effectiveness of antitumor agents [5].

### EXPERIMENTAL METHOD

Three analogous series of experiments were conducted on 118 male golden Syrian hamsters aged 2-3 months. Tumors were induced by introduction of 0.05 ml of a 0.5% solution of DMBA in acetone three times a week in the course of 2 months by means of a probe in the region of the right CP. The CP was examined regularly and scrapings from the mucosa and biopsy material were examined cytologically. After 2 months of the experiment, when small rugose growths 0.1-0.2 cm in diameter were visible in all hamsters against the background of the whitish mucosa, 0.1 ml of physiological saline containing EC of types G<sub>1</sub> and G<sub>2</sub>, without any impurities, began to be applied to the right CP by means of a probe five times a week. The solution was obtained by fractionating a 55-81% alcoholic extract of the epidermis of rat skin by block electrophoresis in agar at pH 5.2 [4]. Each animal received per injection the equivalent of 1 µg protein. Control hamsters received injections of 0.1 ml of physiological saline

TABLE 1. Effect of Chalones on Development of Hamster Cheek Pouch Tumors

Series	Group	Effective number of hamsters*	Mean length of survival, days	Number of hamsters†							
				with no change		with hyperplasia		with papillomas		with carcinoma	
				abso-lute	%	abso-lute	%	abso-lute	%	abso-lute	%
1	Experiment (DMBA + EC)	15	107,7±4,09 ‡	4	26,6	4	26,6	3	20,2	4	26,6
	Control (DMBA)	16	87,9±1,86	0	0	0	0	0	0	16	100
2	Experiment (DMBA + EC)	7	119,4±4,86 ‡	2	28,6	2	28,6	1	14,2	2	28,6
	Control (DMBA)	12	96,1±3,09	0	0	0	0	0	0	12	100
3	Experiment (DMBA + EC)	14	98,8±3,86 ‡	6	42,8	2	14,3	2	14,3	4	28,6
	Control (DMBA)	15	76,9±2,55	0	0	0	0	0	0	15	100

\*Number of hamsters after 8 weeks of experiment.

†Changes in animals which had died or were sacrificed after 4 months. Only the most marked changes were taken into consideration.

‡P < 0.01 compared with control in the given series.

Professor N. N. Petrov Research Institute of Oncology, Ministry of Health of the USSR, Leningrad. (Presented by Academician of the Academy of Medical Sciences of the USSR S. N. Golikov.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 94, No. 11, pp. 68-69, November, 1982. Original article submitted March 23, 1982.

into the right CP. Applications in all groups lasted 4 months. By this time the last control hamsters had died and surviving experimental animals were sacrificed.

#### EXPERIMENTAL RESULTS

Morphological investigation of all the hamsters 8 weeks after the beginning of the experiment revealed papillomas and dysplasia of the epithelium of CP, which later underwent malignant change, leading to the formation of a squamous-cell carcinoma. No metastases of the carcinoma were found. Most of the hamsters died showing disintegration of the tumors and cachexia after 3-4 months of the experiment.

Comparative analysis of the changes in the experimental and control hamsters gave the following results. In the control malignant transformation of precancerous changes and the appearance of malignant tumors were observed in all animals. Meanwhile, after treatment with EC, in some hamsters growth of the neoplasms was delayed and they showed signs of regression, with lengthening of the period of survival of the animals (Table 1). Microscopic study of CP in cases of regression showed only slight evidence of inflammation — the same as in the control hamsters.

The effect observed must be attributed, not to the action of the protein, but to the tissue-specific action of the chalone, for as previous investigations showed [1, 3], hepatic chalone does not affect the development of neoplastic changes in squamous epithelium.

After application of EC to the mucosa of CP in hamsters regression of precancerous changes and inhibition of neoplastic growth are observed. This is evidence of the effectiveness of these substances as inhibitors of tumor growth.

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