Antitumor Action of Kanglaite Injection against Xenograft Human Tumor Models

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Abstract

The antitumor action of Kanglaite Injection against xenograft human hepatoma (QGY), breast carcinoma (Bcap-37), colonic carcinoma (M7609) and lung adenocarcinoma (SPC), was studied in this article. The results showed that Kanglaite Injection could remarkably inhibit tumor growth of above xenograft models. The inhibition rates were 83.78%, 47.40%, 57.14% and 65.08% respectively.
Key Words: Kanglaite Injection, emulsion, nude mouse, human tumor

Antitumor research showed that Kanglaite Injection (KLT) had antitumor action which was significantly effective against the animal transplantable tumors such as Lewis lung carcinoma, W256 carcinosarcoma and B16 melanoma lung metastatic tumor. The purpose of this paper was to investigate the antitumor action of KLT against xenograft human tumor grafted into the nude mice.

1. Materials and method

1.1 Drugs

KLT was supplied by the Pharmaceutical Department of the Traditional Chinese Medicine Hospital of Zhejiang Province, Lot No. 920608, 920721, 940416, 949416.
Cyclophosphamide (CTX) was supplied by Shanghai Hua Lian Pharmaceutical Co. Ltd., Lot No. 910915, 920310.
Dacarbazine (DTIC) was supplied by Nan Jian Pharmaceutical Co. Ltd., Lot No. 940902.

1.2 Tumor cell lines and animals for trial

Human hepatoma (QGY) cell line: Inoculated into BALB/c nude mice, 18-20g, female.
Human breast cancer (Bcap-37) cell line: Inoculated into BALB/c nude mice, 18-20g, female.
Human colon cancer (M7609) cell line: Inoculated into BALB/c nude mice, 18-20g, female.
Human lung adenocarcinoma (SPC) cell line: Inoculated into BALB/c nude mice, 18-20g, female.

The tumor cell lines were kept by the Pharmacological Department of Shanghai Institute of Pharmaceutical Industry.

Nude mice were supplied by the Laboratory Animal Center of Shanghai Institute of Pharmaceutical Industry, HAQC No. 107.

1.3 Antitumor action of KLT against human tumor grafted in nude mice

Tumor tissue of human hepatoma (QGY), breast cancer (Bcap-37), colon cancer (M7609) and lung adenocarcinoma (SPC), acquired from the well-grown tumor implanted at the right axillae of the nude mice, was homogenized and prepared into cell suspension of 1-2´10^7 /ml with normal saline, and subcutaneously inoculated into the right axillae of the nude mice, (0.2ml/mouse). The mice were then grouped randomly and administered with KLT on the next day after inoculation, the dosages were 6.25, 12.5 and 25ml/kg respectively. The positive control group was administered with CTX or DTIC, while the negative control group with the vehicle. The inhibition rate was calculated based on the tumor weights of the animals that were sacrificed about 30 days after inoculation.

2. Results

2. 1 Antitumor effect of KLT against grafted human hepatoma (QGY) in the nude mice

The results showed that KLT, at the dosage of 6.25, 12.5 and 25ml/kg intravenously, could significantly inhibit the growth of human hepatoma (QGY) grafted in the nude mice. The inhibition rates were 49.55, 69.73 and 83.78% respectively. Furthermore the effect was intensified with the dose increasing, and the inhibition rate could approach to that of the positive control (CTX) when the dose was high enough. Body-weight declining and evident toxic reactions could be observed among the nude mice in CTX group, while no such symptoms were found in the KLT groups. (Table 1).

Table 1. Antitumor effect of KLT against human hepatoma (QGY)

Drug	Dose ml/kg	Administration Scheme	Animal No.		Body weight of Animal (g)		Tumor weight (g)	Inhibition Rate (%)
			Start	End	Start	End	X±SD	
Control	25.0	iv×10	5	5	20.1	21.7	3.33±0.86	
KLT	6.25	iv×10	5	5	19.4	20.9	1.68±0.53**	49.55
KLT	12.5	iv×10	5	5	19.8	21.2	1.02±0.31**	69.37
KLT	25.0	iv×10	5	5	19.7	20.9	0.54±0.22**	83.78
CTX	30mg/kg	ip×10	5	5	19.9	19.1	0.28±0.08**	91.59

Comparing with the control group: **P<0.01

2.2 Antitumor effect of KLT against grafted human Breast cancer (Bcap-37) in the nude mice

The results showed that KLT, at the dosage of 6.25, 12.5 and 25ml/kg intravenously, could significantly inhibit the growth of human Breast cancer (Bcap-37) grafted in the nude mice. The inhibition rates were 22.54, 35.26 and 47.40% respectively. And the effect was intensified with the dose increasing. (Table 2).

Table 2. Antitumor effect of KLT against human breast cancer (Bcap-37)

Drug	Dose ml/kg	Administration Scheme	Animal No.		Body weight of Animal (g)		Tumor weight (g)	Inhibition Rate (%)
			Start	End	Start	End	X±SD	
Control	25.0	iv×7	6	6	19.5	21.0	1.73±0.26	
KLT	6.25	iv×7	6	6	19.6	21.0	1.34±0.30*	22.54
KLT	12.5	iv×7	6	6	19.3	20.5	1.12±0.21**	35.26
KLT	25.0	iv×7	6	6	19.5	20.8	0.91±0.13**	47.40
CTX	30mg/kg	ip×7	6	6	19.5	19.6	0.12±0.04**	93.06

Comparing with the control group: **P<0.01，*P<0.05.

2.3 Antitumor effect of KLT against grafted human colon cancer (M7609) in the nude mice

The results showed that KLT, at the dosage of 6.25, 12.5ml/kg intravenously, could significantly inhibit the growth of human colon cancer (M7609) grafted in the nude mice. The inhibition rates were 35.71, 57.14% respectively. And the effect was evidently intensified with the dose increasing. (Table 3)

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Table 3. Antitumor effect of KLT against human colon cancer (M7609)

Drug	Dose ml/kg	Administration Scheme	Animal No.		Body weight of Animal (g)		Tumor weight (g)	Inhibition Rate (%)
			Start	End	Start	End	X±SD	
Control	12.5	iv×7 (9-15)	6	6	19.7	21.2	1.40±0.36	
KLT	6.25	iv×7 (9-15)	6	6	19.4	21.1	0.90±0.10**	35.71
KLT	12.5	iv×7 (9-15)	6	6	19.3	20.4	0.60±0.35**	57.14
CTX	100mg/kg	ip×2 (9,11)	6	6	19.6	19.4	0	100

Comparing with the control group: **P<0.01

2.4 Antitumor effect of KLT against grafted human lung adenocarcinoma (SPC) in the nude mice

The results showed that KLT, at the dosage of 6.25, 12.5 and 25ml/kg intravenously, could significantly inhibit the growth of human lung adenocarcinoma (SPC) grafted in the nude mice. The inhibition rates were 23.81, 42.85 and 65.08% respectively, and the effect was evidently intensified with the dose increasing (Table 4).

Table 4. Antitumor effect of KLT against human lung adenocarcinoma (SPC)

Drug	Dose ml/kg	Administration Scheme	Animal No.		Body weight of Animal (g)		Tumor weight (g)	Inhibition Rate (%)
			Start	End	Start	End	X±SD	
Control	25.0	iv×10	6	6	19.2	21.0	2.52±0.43	
KLT	6.25	iv×10	6	6	19.0	20.5	1.92±0.22*	23.81
KLT	12.5	iv×10	6	6	19.3	20.7	1.44±0.31**	42.85
KLT	25.0	iv×10	6	6	19.2	20.4	0.88±0.19**	65.08
DTIC	40mg/kg	iv×10	6	6	19.1	19.0	0.13±0.05**	94.84

Comparing with the control group: **P<0.01，*P<0.05

3. Discussion

The major drawback of the animal transplantable tumor as the most common model in the Screening Test is the inconsistency of experimental results with its clinical reactions. Antitumor drugs discovered by using animal transplantable tumor were effective mainly for malignant lymphoma and leukemia based on previous experience, yet clinically had poor efficacy on solid tumors such as pulmonary carcinoma, hepatic carcinoma, gastric carcinoma and esophagus carcinoma etc. The antitumor action of KLT against human hepatoma (QGY), breast cancer (Bcap-37), colon cancer (M7609) and lung adenocarcinoma(SPC) grafted in the nude mice was studied in this paper. The results demonstrated that the antitumor emulsion-KLT Injection could significantly inhibit the growth of the above tumors. Besides, its action could be intensified with the dose increased, reveling an evident dosage activity relationship.

References

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