中國1號天仙液 對移植性S\textsubscript{180}肉瘤和肝癌抑制作用的研究

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The Study on the Inhibition Effects of FRC001 (China No.1 Tian Xian Liquid) on Tansplatation Sarcoma S180 and Hepatocarcinoma

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ABSTRACT
The transplation sarcoma S180 and hepatic carcinoma of mouse are the most popular and important models in the screening of antineoplastic drugs. This paper studied the inhibition effects of FRC001 on these two models. The results showed that on FRC001 had inhibition effects, to some extent, sarcoma S180 and hepatic carcinoma. Among then, the inhibition rate of high, middle and low dose of FRC001 on S180 were 59.73%, 52.57%, 41.33%, respectively which showed obvious dose-dependent effects; FRC001 also had some effects on hepatic carcinoma foci, and the inhibition rate was 47.81%; after the treatment of FRC001, the average weight decreased and the carcinoma foci shranked apparently compared with the control group (P<0.05 or P<0.01). FRC001 is an antineoplastic using traditional Chinese medicine as the main ingredient.

Key Words: FRC001, Transplation tumor, Sarcoma S180, Inhibition effect on hepatic carcinoma

BACKGROUND
Malignant tumor is a series of commonly encountered diseases which harm the human. The treat­ment of it is a difficult problem of today's world medical science. Besides operation, radiotherapy, chemotherapy, the roles of TCM and the combination of Chinese and Western medicine are widely noted by medical circles. FRC001 is prepared mainly using traditional Chinese drugs which can eliminate the pathogenic factor and support healthy energy. The supporting healthy energy includes invigorating Qi and enriching the blood, warming Yang and nourishing Yin; the eliminating the pathogenic factor includes promoting blood circulation to remove stasis, clearing away heat and toxic material and softening and resolving hard mass. These methods have better inhibition effect on tumors.

This paper studied the effects of FRC001 on transplation carcinoma S180 and hepatic carcinoma of mice.

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MATERIALS AND METHODS

1. Materials

1.1 Test Drug: FRC001 (liquid extract of Chinese drugs), provided by China-Japan Feida Union Co., LTD.

1.2 Experimental Animal: mouse, pure Kunming bred C57BL/6J, 18-22g, healthy, 2-3 months, male and female, provided by Experimental Animal Center of Jiangsu Tumor Prophylactic-therapeutic Research Institution.

1.3 Test Tumor Strain: ① Sarcoma S180 strain; ② Hepatic carcinoma strain, provided by Medicine Research Department of Jiangsu Tumor Prophylactic-therapeutic Research Institution.

2. Methods of Preparing Animal Pattern

2.1 Sarcoma S180

Ascites S180 sarcoma were drawn from mice in which S180 had been inoculated 7-9 days ago, diluted by normal saline to be 1 × 10^6/ml sarcoma cell solution. The next day, mice were inoculated the sarcoma cell solution 0.2 ml subcutaneously in their right forefeet by aseptic manipulation; then were randomly grouped and put into experiment. The mice were endogastrically given drugs such as FRC001, etc, one time daily for successive 12 days, and dissected to get sarcoma on the 13th day. The sarcoma were weighted precisely (g), and calculate the inhibition rates of drugs on sarcoma by following formula:

\[
A\% = \frac{X - Y}{X} \times 100\%
\]

Where:
- \( A\% \) - Inhibition rate of FRC001 on sarcoma S180;
- \( X \) - The average S180 weight of control group (g);
- \( Y \) - The average S180 weight of experimental group.

2.2 Hepatic Carcinoma:

Hepatic carcinoma strain was diluted to 1 × 10^6/ml carcinoma cell suspension solution by normal saline. The mice were inoculated above carcinoma solution 0.2ml in their right forefeet by aseptic manipulation. The next day, they were randomly grouped and given drug such as FRC001, etc/one time daily for successive 8 days, and dissected on the 9th day. The body weight and hepatocarcinoma weight were got accurately. To calculate the inhibition rates of drugs on hepatic carcinoma by following formula:

\[
C\% = \left(1 - \frac{W}{Z}\right) \times 100\%
\]

Where:
- \( C\% \) - Inhibition rate of drug on hepatic carcinoma;
- \( W \) - Average hepatocarcinoma weight of experimental group (g);
- \( Z \) - Average hepatocarcinoma weight of control group (g).

RESULTS AND DISCUSSION

1. The inhibition effect of FRC001 on transplantation Sarcoma S180 of mice:

To explore the dose-effect of FRC001 on S180 and find the optimal dose, we tested three doses, i.e. high dose (6.0ml/kg.bw), middle dose (3.0ml/kg.bw) and low dose (1.5ml/kg.bw) of FRC001 on
Table 1. The Effects of FRC001 on Transplantation Sarcoma S180 of Mice

<table>
<thead>
<tr>
<th>Group</th>
<th>Number (n)</th>
<th>Dosage (ml/kg.bw)</th>
<th>Experiment Days (d)</th>
<th>Average Weight of S180 (X±SD)</th>
<th>Inhibition Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Group</td>
<td>10</td>
<td>0</td>
<td>12</td>
<td>3.75±1.53</td>
<td>-</td>
</tr>
<tr>
<td>High Dose</td>
<td>10</td>
<td>6.0</td>
<td>12</td>
<td>1.51±0.43***</td>
<td>59.73</td>
</tr>
<tr>
<td>Middle Dose</td>
<td>10</td>
<td>3.0</td>
<td>12</td>
<td>1.78±0.58***</td>
<td>52.53</td>
</tr>
<tr>
<td>Low Dose</td>
<td>10</td>
<td>1.5</td>
<td>12</td>
<td>2.20±0.93**</td>
<td>41.33</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>10</td>
<td>25mg/kg.bw</td>
<td>12</td>
<td>1.96±1.00***</td>
<td>47.73</td>
</tr>
</tbody>
</table>

Compared to control group, *P>0.05; **P<0.05; ***P<0.01; ****P<0.001

Figure 1. Dose-effect Curve of FRC001 on S180

According to Table 1, three doses of FRC001 had different inhibition effects on transplantation Sarcoma S180 of mouse. The average weights of S180 of the three doses were significantly smaller than that of control group (P<0.05 or P<0.01). These findings showed that FRC001 had some inhibition effect on sarcoma S180.

According to Figure 1, the inhibition of FRC001 on transplantation sarcoma S180 of mouse were dose-dependent, i.e., as the increasing of the dose of FRC001, the inhibition effects on S180 enhanced, the weight of sarcoma decreased and the foci shrunked.
On the basis of the dose-effect research, high dose of FRC001 (6.0ml/kg.bw) was chosen to test and its effects on the body weight, carcinoma weight of experimental animal of hepatic carcinoma and the inhibition rate were investigated (showed in Table 2 and Figure 3,4).

According to Table 2, these drugs had some inhibiton effects on hepatic carcinoma foci of experimental animals which showed in the decrease of carcinoma weights. The average carcinoma weights of drug I - VI were 1.41g,1.09g,1.26g,1.49g,1.02g,0.71g, respectively, decreased 0.65g,0.97g,0.80g,0.59g,0.104g,1.35g, respectively compared with control group. Compared to the control group, the effects of drug I, IV were not significant statistically (P>0.05), whereas drug II, III, V, VI had significant effects (P<0.01 or P<0.001).

Figure 3 showed that the carcinoma weight of control group was the biggest, the carcinoma weights of drug I - VI decreased to some extent, but there were carcinoma foci in all drug groups. The orders of carcinoma weights of all experimental groups: Control>drug IV>drug I >drug III >drug II >drug V >drug VI.

Figure 4 showed these drugs had some inhibition effects on carcinoma foci. According to the antineoplastic screening procedures and standards that the inhibition rate must be up to 30%, except for drug IV (27.67%), all drugs had good inhibition effects. The orders of inhibition rates of drug I - VI: drug VI >drug V >drug II >drug III >drug I >drug IV. Drug VI is 5-Fu which is one of the chemotherapeutic drugs having good antineoplastic effect. Drug V is a new complex preparation of Chinese and Western drugs which is being screened by author. Drug II is a marketing antineoplastic, and its effect is weaker than drug VI and V.

These results showed that, as an antineoplastic, FRC001 had some effects on sarcoma S180 and hepatic carcinoma. The mechanisms may be: (1) FRC001 is a complex preparation of Chinese and Western drugs, can promote blood circulation to remove stasis, clear away heat and toxic material, soften and resolve hard mass, invigorate Qi, enrich the blood, warm Yang and nourish Yin, so it can help body to eliminate the pathogenic factor and support healthy energy, clear away toxic material and resist tumors; (2) The components in Edfrann may have the function of invigorating Qi, spleen, resolving dampness, soothing the liver and regulating the circulation of Qi, digestant, regulating absorption, eliminating disturbance of substance metabolism, enhancing circulation, hemopoiesis, immunity, and can regulate the function of nerve, endocrine, electrolyte, cyclic nucleoside, etc; (3) FRC001 can inhibit the growth of tumor by regulating immunologic function, enhancing the phagocytic function of reticuloendothelial system; (4) FRC001 maybe has the function of inhibiting the metabolism of RNA and DNA of carcinoma cell so as to kill the carcinoma cell or inhibit the growth of carcinoma cell; (5) FRC001 maybe has the function of eliminating free radicals, as the free radicals play an important role in mutagenesis and carcinogenesis. FRC001 contains macromolecule and micronolecule radical scavenge. Of course, the growth, development or inhibition is a complicated biologic course, the effects and accurate mechanism of FRC001 on tumor are awaited to further study.

REFERENCES

[4] Li Xuetang, Clinical Trial of Anticarcinogen, Cancer 1989,8 (2):116-117

(6) Sun Zhij Yong, Active Oxygen and Carcinogenesis, Abroad medicine (Tumor) 1990,19 (2) :65

(7) Han Zhihong, Liu Xiaokang, Wu Yongfang, The Effects of green Tea Extracts TP-91 on S180 of Mouse and the Activity of SOD in RBC, Free Radicals Bioscience Progress. 1995,3 (3) :182

(8) Zhu Jian-hong, et al. preclinal trials with monoclonal antibody immunoconjugate for the tragecing chemotherapy of human brain glioma. 9th Int. congress of neurological surgery october, 1989.new Delhi-India. Resident's Award Papers.No. 8000001

(9) Rayner AA. et al. Lymphokine-Activated killer (LAK) cells Analysis of factors relefv ant to the immunotherapy of human cancer. cancer, 1989;55:1327


(14) Goldsmith MA et al. Quantitative Prediction of drug toxicity inhuman from toxicology in small and large animals cancer Res. 1975;35:1354-1364


(17) Xie Bingfen, Pan Qichao, Cheng Haiying, et al. The Relation of Methionine with the Growth of Transplantation Carcinoma of Mouse and the Action of Anticarcinogen, Cancer, 1989,8 (6) :438-441

(18) Zhu Yingeng, et al. The pathologic Effects of Pretreatment of Hepatocarcinoma Vaccine on Transplantation Hepatocarcinoma of Mouse, Tumor Protective and Treatment Research, 1984,11 (1) :1


(20) Yan Ruiqi, et al. The Inhibition of Green Tea on Hepatocarcinoma of Rat Induced by Aflatoxin B1, Cancer 1987, 6 (2) :83


(22) Marks PA et al. Report from Memorial Sloan-Kettering Cancer center, 1986;184.


Cancer Res, 1987,47-4093.

[28] Connolly KM, Bogdanffy MS. Evaluation of proliferation cell nuclear antigen (PCNA) as an endogenous marker of cell proliferation in rat liver: a dual stain comparison with 5-bromo-2'-deoxyuridine. J Histochem Cytochem, 1993,41:1


