Immunological analysis of inhibition of lung metastases by fucoidan (GIV-A) prepared from brown seaweed Sargassum thunbergii.

Itoh H, Noda H, Amano H, Ito H.

Laboratory of Marine Biochemistry, Faculty of Bioresources, Mie University, Tsu, Japan.

The antimetastatic effect of GIV-A (fucoidan) and/or 5-FU was examined in an experimental model of lung metastases induced by Lewis lung carcinoma in mice. Injection of GIV-A i.p. after removal of the implanted primary tumor inhibited the development of lung metastases. Combination treatment with GIV-A and 5-FU inhibited significantly the lung metastases. The number of peritoneal macrophages, total cells and macrophages in the lung increased in mice treated with GIV-A. Binding of the third component of complement (C3) cleavage products (C3b) to the C3 receptor on peritoneal macrophages after i.v. injection of GIV-A was enhanced, as shown by the fluorescent antibody technique. Lung metastases were inhibited by i.v. injection of peritoneal macrophages activated with GIV-A. GIV-A depressed aniline hydroxylase and aminopyrine demethylase activities of the hepatic microsomal drug-metabolizing system in tumor-bearing mice. Moreover, the concentration of 5-FU in the tissues (lung, liver, kidney, spleen and blood) was increased significantly by coadministration of GIV-A. The picryl chloride-induced delayed type hypersensitivity (PC-DTH) response in mice was depressed after the implantation of tumor and treatment with 5-FU. GIV-A restored the suppression of PC-DTH by 5-FU, but did not increase the PC-DTH of normal mice. GIV-A not only enhanced the degree of spleen cell-mediated sheep red blood cell (SRBC) hemolysis (quantitative hemolysis of SRBC), the indexes of the spleen and thymus and the number of spleen cells, but also restored the suppressive effect of 5-FU. In the group receiving GIV-A, the percentages of splenic Thy1.2-, L3T4- and asialo GM1-positive cells were significantly increased as compared with the tumor-bearing mice treated with saline. Furthermore, the L3T4+/Lyt2+ ratio showed a tendency to increase, and the Lyt2+/Thy1.2+ ratio was decreased. These results suggest that the antitumor effect of GIV-A may be correlated with the changing pattern of the Thy1.2-, L3T4- and asialo GM1-positive cells, C3 activation, macrophage activation and depression of the hepatic microsomal drug-metabolizing system. These findings raise the possibility that GIV-A may have clinical value in the prevention of cancer metastasis.

PMID: 8572581 [PubMed - indexed for MEDLINE]