

The effect of the flavonoid diosmin, grape seed extract and red wine on the pulmonary metastatic B16F10 melanoma

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Summary. Objective: To study the effect of different phenolic compounds and red wine on pulmonary metastatic melanoma. Methods: Swiss mice were inoculated with 5×10^5 melanocytes B16F10 and given oral doses of diosmin, grape seed extract (GSE) and red wine. A macroscopic count was made of the metastatic nodules on the lung surface and a microscopic study by image analysis of five sections, calculating the implantation percentage and tumoral growth and invasion indices. Results: Macroscopically, the group treated with diosmin showed the greatest reduction (52%) in the number of metastatic nodules compared with the control group, which was treated with ethanol, while GSE and red wine caused decreases of 26.07 and 28.81%, respectively. Microscopically, there was a decrease in the implantation percentage after the administration of diosmin (79.4%) and red wine (20.19%), and an increase of 2.12% after the administration of GSE, all relative to the ethanol-treated control. As regards the growth index, diosmin produced a reduction of 67.44% and red wine a reduction of 20.62%, while GSE again produced an increase (25.33%). The reductions in the invasion index were 45.23, 31.65 and 17.57% with diosmin, GSE and red wine, respectively. Conclusions: Diosmin originated the greatest reduction in pulmonary metastases, both at the macroscopic and microscopic levels.

Key words: B16F10, Pulmonary metastasis, Procyanidins, Flavonoids, Diosmin

Introduction

Melanoma is a serious challenge in oncology because of the ineffectiveness of known treatments and the progressive increase in mortality recorded in fair skinned people from all over the world (Holme et al., 2001). Despite representing only 4% of skin cancers, it is responsible for 80% of skin cancer deaths (Horn-Ross, 2003), most as a consequence of metastasis. It is one of the neoplasias that metastasise most frequently, especially in the lymphatic glands or the lung. In the latter organ, it occurs with a frequency of between 12.2% (Harponne et al., 1992) and 20% (Majeski, 1999). Pulmonary metastasis constitutes one of the most important causes of death in oncological patients (Kumar et al., 2004). The difficulty of treating metastases lies in the interactions between tumoral cells and the homeostatic mechanisms that replace them (Fidler, 2002). They show one of the worst response rates to chemotherapy, basically due to the resistance of cells to antineoplastic agents (Helmbach et al., 2001) and also because of the secondary problems, which are common. Hence, the interest in finding new antimetastatic agents; in this sense, some polyphenolic compounds have been described as potentially chemoprotective dietary agents against cancer (Miller et al., 1994). Numerous epidemiological studies have suggested that the consumption of fruit and vegetables, besides having other benefits, reduces the risk of cancer due to the polyphenolic compounds they contain (O'Brien, 2001). For its part, diosmin is a flavonoid widely used in medicine as an antivaricose agent and vasoprotector.

Epidemiological studies have suggested that the low incidence of coronary heart disease in France is due to the protective effect of red wine ("the French paradox")