Abstract:

Hesperidin, a flavonoid found mainly in citrus, was reported to inhibit growth and proliferation of several cancers, including colon cancer cells. However, the question does p53 tumor suppressor protein is required for the effect of hesperidin is not yet clarified. In the present study, the effect of hesperidin on p53-expressing (HCT116 p53+/+) and p53-knockout (HCT116 p53-/-) human colon cancer cells was investigated. Hesperidin inhibits cell growth of both HCT116 p53+/+ and HCT116 p53-/ cells, however, it was more effective in p53-expressing cells. Hesperidin induced G1 cell cycle arrest in only HCT116 p53+/+ cells however induction of reactive oxygen species (ROS) and apoptosis was induced in both cells. Furthermore, hesperidin activates the proapoptotic (Bax) and cyclin dependent kinase inhibitor (p21) in only HCT116 p53+/+ cells. Interestingly, using p53 transcriptional inhibitor (pifithrin-a), hesperidin-inducing Bax and p21 upregulation in only HCT116 p53+/+ cells was reduced by cotreatment with pifithrin-a without inducing any changes in HCT116 p53-/ cells. Altogether; these results showed that hesperidin induced apoptosis and G1 cell cycle arrest in colon cancer cells in a p53/Bax -- dependent and -- independent, and p53/p21 - dependent manners; respectively.

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