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Hwanggeumchal sorghum induces cell cycle arrest, and suppresses tumor growth and metastasis through the down-regulation of Jak2/STAT pathways in breast cancer xenografts

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Objectives

Cancer is one of the most virulent diseases known to humankind with high mortality rate. Colon cancer is common cancer in worldwide. Hwanggeumchal Sorghum is a principal cereal food crops in many parts of the world, and is critical in folk medicine of Asia and Africa. In the present study we analyzed the effects of HSE in metastatic colon cancer management. Studies conducted on Balb/c nude mice xenograft models showed tumour growth suppression by HSE.

Materials and Methods

○ Tumorigenicity

All procedures for animal experiments were approved by the Committee on the Use and Care on Animals (Institutional Animal Care and Use Committee, Seoul, Korea) and performed in accordance with the institution guidelines. HCT 116 tumor xenografts were established by subcutaneously inoculating 1×10^7 cells into the right flank of 5-week-old BALB/c nude mice (Orient Bio, Seongnam-Si, Korea). When tumors reached between 6 to 8 mm in diameter, mice were randomly assigned to control group, HSE 0.01%-treated group and HSE 0.02%-treated group, respectively with 6 mice in each group. The drug was administered as intragastric injections of 100 μl, containing 0.01% HSE or 0.02% HSE in triple distilled water. The injections were repeated one time every other day. Tumor growth was monitored by periodic measurements with calipers. Tumor volume was calculated using the formulae:

Tumor volume (mm^3)=maximal length(mm)×(perpendicular width)$(mm)^2$/2.

Animals were sacrificed when the diameter of tumors reached 2 cm or after 30 days of treatment. In our experiments, no mice were observed to be died of tumor loading. All available colon cancer specimens collected from in human colon cancer xenograft mice were reviewed and included in the study. Mice were euthanized and the tumors were removed. The tumors were fixed with 4% paraformaldehyde followed by paraffin embedding and sectioning (5 μm).

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Results

The rate of tumor growth in untreated mice (100% vehicle, n = 6) was significantly greater than that in mice treated with 10 mg HSE /kg body weight (50.2%, n = 6) (Fig. 1). Immunohistochemistry (IHC) conducted on both in vivo and in vitro samples showed that HSE can modulate Jak/STAT pathways. HSE hindered the STAT5b/IGF-1R and STAT3/VEGF pathways by down-regulating the expression of these signal molecules. The expression of angiogenic factors like VEGF was found down-regulated by HSE (Fig. 2).

Usage of HS as a dietary supplement is an inexpensive natural cancer therapy, without any side effects. We strongly recommend the use of HS as an edible therapeutic agent as it possesses tumor suppressive effects on colon cancer

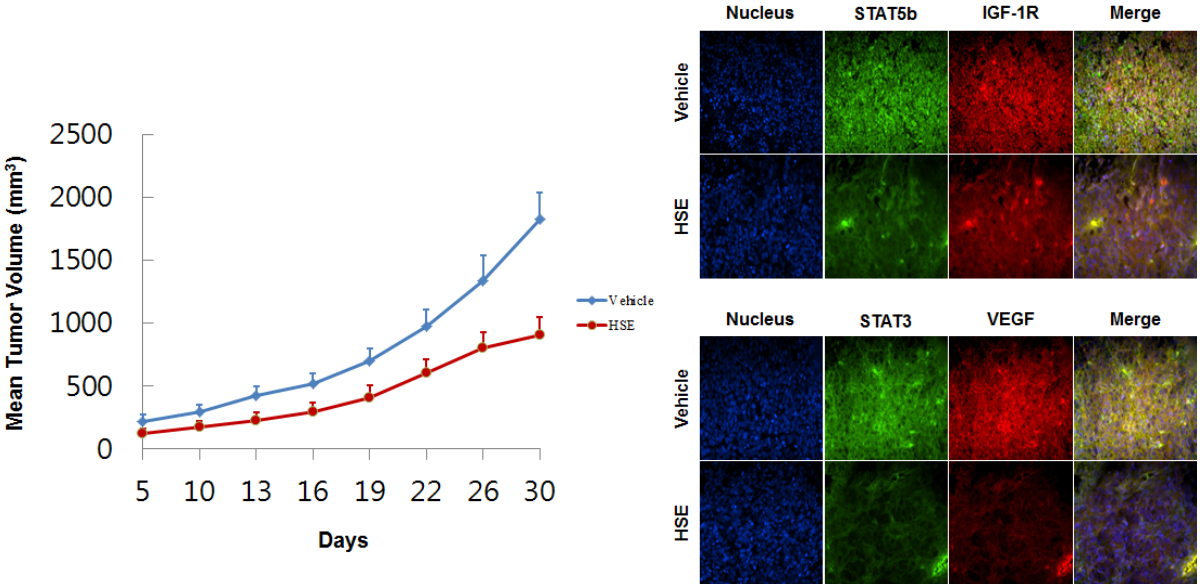

Figure 1. HSE suppressed the growth of human colon cancer xenograft in mice.

Figure 2. HSE down-regulated STAT5b/IGF-1R and STAT3/VEGF signal pathway.