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Antitumor Effects of a Mushroom–Genistein Combination on Prostate Cancer

Robert M. Hackman,[1] Buxiang Sun,[2] and Ralph W. de Vere White[3]

[1]Department of Nutrition, University of California at Davis, Davis, CA 95616, USA; [2]Amino Up Chemical Co., Ltd., Sapporo 004-0839, Japan; and [3]Department of Urology, University of California at Davis, Davis, CA 95616, USA

Mushrooms have been used traditionally to treat many types of cancers. Genistein is an isoflavone from soy and other plants that may also have benefit for cancer treatment and prevention. The aglycone forms of isoflavones (such as genistein) are thought to be primary active compounds, but plants contain isoflavones primarily in their glucoside forms, which are poorly absorbed. Supplemental aglycones raise serum isoflavone levels twice as much as do glucosides, and may have therapeutic value in humans. Aglycones are difficult to produce. A unique feature of shiitake mushrooms is their level of β-glucosidase, the enzyme that converts glucoside isoflavones to their more potent aglycone forms. Soy was cultured with shiitake mushroom mycelia, resulting in a 10× increase in genistein. The final product (GCP) was also rich in active glucans from the mushrooms. Six human cancer cell lines and two mouse carcinoma cell lines were studied *in vitro*. Four were derived from prostate (LNCaP, PC3, DU145, and TSU-pr1); one from bladder (T24); and one each from bone (Saos-2), lung (3LL), and colon (Colon 26). GCP inhibited growth of all cell lines in a dose-dependent manner. GCP was found to down-regulate VEGF expression in some cell lines and to induce apoptosis in PC3, 3LL, and T24 cells. Nude mice implanted with PC3 cells and fed GCP showed significantly reduced tumor growth compared to those fed a control diet ($p < 0.002$). GCP was also tested when given in combination with another shiitake mushroom extract (AHCC). Combined GCP+AHCC treatment induced more obvious apoptotic deaths than either ingredient alone using both *in vitro* and *in vivo* models. Synergistic inhibitory effects were also found on tumor growth of 3LL or Sarcoma 180 tumors grown in C57/BL6 and FVB mice, respectively. Nude mice implanted with PC-3 bearing tumors and fed a combination of GCP+AHCC showed significantly slower tumor growth compared to nonsupplemented animals. When the GCP+AHCC was withdrawn, the rate of tumor growth accelerated dramatically. On reintroduction of GCP+AHCC to the mice, tumor growth was again slowed. A high genistein and shiitake mushroom combination demonstrated significant antitumor effects. Addition of the novel mushroom extract appeared to improve the response further.

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