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GCP (GENISTEIN CONCENTRATED POLYSACCHARIDE): A SOYBEAN ISOFLAVONE DIETARY SUPPLEMENT FERMENTED BY BASIDIOMYCETES WITH ANTICARCINOGENIC ACTIVITIES: THEIR MOLECULAR MECHANISMS AND CHEMOPREVENTIVE POTENTIAL

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GCP is a novel functional food obtained from the extracts of soybean isoflavone fermented with basidiomycetes mycelia. The enzyme reaction makes GCP containing high concentration of isoflavone aglycons, particularly for genistein and high content of polysaccharides. GCP exerts its anti-tumor activities by anti-angiogenesis and induction of apoptosis in cancer tissues and by enhancement of immune responses in immune system. We revealed GCP inhibited angiogenesis by several experiment models including a rat aortic ring model *in vitro*; a chick chorioallantoic membrane ex ove; and a rat mesenteric windows model *in vivo*. We also demonstrated that GCP induced cancer cells to apoptosis by Annexin V assay, TUNEL staining and DNA fragmentation analysis. Cell cycle analysis showed GCP significantly decreased the cells in G1S phase. Western blot analysis showed apoptosis related protein p 53 and p21 ^{waf1} involved in the apoptosis process. GCP inhibited significantly primary tumor and metastasis to lung in diethylnitrosamine-initiated and phenobarbital-promoted hepatocarcinogenesis model. A human monitor test showed serum genistein reached about 4 μg/ml after 3 hours of oral administration of GCP (2 g). This serum concentration of genistein had no side effect to the health people, while *in vitro* the same concentration of genistein had significant cytotoxicity to cancer cells. The further study found genistein exists as a conjugated genistein glucuronide complex in system circulation, the conjugated genistein could not exert any physiological

activity. Our data revealed most of tumor tissues and angiogenesis areas produce high amounts of β-glucuronidase, the enzyme could transferred conjugated genistein glucuronide complex into genisten aglycone in tumor or angiogenesis local areas. The genistein aglycone exerts high cytotoxicity to tumor cells and new blood vessels. This effect resulted in finally the tumor regression revealed in different tumor bearing models. The data described above indicated GCP is a potential anti-carcinogenic and chemopreventive dietary supplement.