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File: ■ Monk Fruit [*Siraitia grosvenorii (Swingle)*, Cucurbitaceae]
■ Mogroside V
■ Pancreatic Cancer

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RE: Mogroside V, a Compound of Monk Fruit, Inhibits Pancreatic Cancer Cell Proliferation and Promotes Tumor Apoptosis In Vivo and In Vitro

Liu C, Dai LH, Dou DQ, Ma LQ, Sun YX. A natural food sweetener with anti-pancreatic cancer properties. *Oncogenesis*. April 2016;5:e217. doi: 10.1038/oncsis.2016.28.

Much oncology research involves searching for more effective and less toxic chemotherapy drugs. Screening of plants for bioactive compounds can supply drug development leads, but is costly and time-consuming. These authors suggest that plants with long histories of medicinal use, such as those used in Chinese medicine, should be prioritized for study. Among those plants is monk fruit [luo han guo; *Siraitia grosvenorii (Swingle)*, Cucurbitaceae]. According to the article, the *Pharmacopoeia of the People's Republic of China* lists the benefits of monk fruit as "heat-releasing and lung-moistening," relieving throat and vocal problems, and laxative activity.

Monk fruit saponins were approved in 1997 by the Chinese Ministry of Health for use as a sweetener in foods. The effect of these compounds in pancreatic cancer was of interest because patients with that disease should limit sugar intake, and might substitute other natural sweeteners. In this study, these authors examined the effects of mogroside V (Sigma-Aldrich; St. Louis, Missouri), a triterpene glycoside, on the proliferation and viability of PANC-1 (human pancreatic carcinoma, epithelial-like) cells (Shanghai Cell Biology Institute; Shanghai, China) in vitro and in vivo.

PANC-1 cells were incubated with mogroside V at concentrations of 0 µmol/L to 250 µmol/L. The MTT assay, terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assays, and flow cytometry were used to measure proliferation and apoptosis. Several other cell lines were subjected to comparable MTT assays. Western blot assays were used to examine the effects on the signal transducer and activator of transcription 3 (STAT3) signaling pathway, which contributes to cell growth and proliferation and may be involved in the development of several types of cancer.[1,2]

In vivo activity was assessed in a xenograft model in which eight-week-old male BALB/c mice (Charles River Ltd. Co.; Beijing, China) were subcutaneously injected with PANC-1 cells. Five groups of six mice were treated three times weekly with 2, 10, or 30 mg/kg

body weight of intravenous mogroside V, normal saline, or no treatment. Tumor volumes were estimated every five days from measurements with calipers; after five weeks, the mice were sacrificed, tumors were weighed and measured, and vascularization was examined in stained sections. Real-time polymerase chain reaction was used in fresh tumor tissue to measure expression of *PCNA* and *Ki-67*, markers of tumor cell proliferation, and paraffin-embedded sections were stained using monoclonal antibodies for those genes.

Results revealed that mogroside V reduced proliferation and increased apoptosis in PANC-1 cells and most of the other cell lines tested; the effect was both concentration- and time-dependent. (The only cell line that showed very little reduction in cell proliferation, CFPAC-1, was another of the pancreatic adenocarcinoma lines tested.) Treatment of PANC-1 cells with mogroside V reduced phosphorylation of STAT3 and two kinases upstream of STAT3 in the same pathway, increasing expression of two cyclin kinase inhibitors, associated with cell cycle arrest, and two pro-apoptotic proteins.

In the mouse xenograft model, all doses significantly reduced tumor growth, with higher doses more effective, and survival to the end of the study was improved. Mean tumor volume, based on postmortem measurement, was stated to be 278.6 ± 0.03 mm^3 in control mice versus 56.4 ± 0.11 mm^3 in the mice receiving 30 mg/kg doses of mogroside V ($P<0.001$). Tumor weight in the same groups was 32.2 ± 1.4 g versus 9.2 ± 1.8 g ($P<0.001$). Expression of *PCNA* and *Ki-67* in tumor tissues was significantly reduced with mogroside V treatment ($P<0.001$ for all doses relative to the control group, with higher doses most effective). Mogroside V also inhibited angiogenesis and the expression of vascular endothelial growth factor (VEGF), which plays a role in angiogenesis,[3,4] with the highest dose most effective ($P<0.001$ vs. control).

Mogroside V may act against pancreatic cancer by multiple mechanisms, increasing apoptosis while inhibiting cell proliferation and angiogenesis, perhaps in part by inhibiting the STAT3 pathway. In future studies, the authors plan to investigate this further by exploring the efficacy of mogroside V when STAT3 is stably overexpressed or deleted in the PANC-1 cells used in xenografts. The authors say that mogroside V has been approved by the United States Food and Drug Administration as a sweetener, and suggest that its use might reduce the risk of pancreatic cancer. [Note: A March 2016 Generally Recognized as Safe (GRAS) notice for *S. grosvenorii (Swingle)* fruit extract is listed as "pending" as of this writing.]

—Shari Henson

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The American Botanical Council has chosen not to reprint the original article.