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Celery, artichokes contain flavonoids that kill human pancreatic cancer cells

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Celery, artichokes, and herbs, especially Mexican oregano, all contain apigenin and luteolin, flavonoids that kill human pancreatic cancer cells in the lab by inhibiting an important enzyme, according to two new University of Illinois studies.

"Apigenin alone induced cell death in two aggressive human pancreatic cancer cell lines. But we received the best results when we pre-treated cancer cells with apigenin for 24 hours, then applied the chemotherapeutic drug gemcitabine for 36 hours," said Elvira de Mejia, a U of I professor of food chemistry and food toxicology.

The trick seemed to be using the flavonoids as a pre-treatment instead of applying them and the chemotherapeutic drug simultaneously, said Jodee Johnson, a doctoral student in de Mejia's lab who has since graduated.

"Even though the topic is still controversial, our study indicated that taking antioxidant supplements on the same day as chemotherapeutic drugs may negate the effect of those drugs," she said.

"That happens because flavonoids can act as antioxidants. One of the ways that chemotherapeutic drugs kill cells is based on their pro-oxidant activity, meaning that flavonoids and chemotherapeutic drugs may compete with each other when they're introduced at the same time," she explained.

Pancreatic cancer is a very aggressive cancer, and there are few early

symptoms, meaning that the disease is often not found before it has spread. Ultimately the goal is to develop a cure, but prolonging the lives of patients would be a significant development, Johnson added.

It is the fourth leading cause of cancer-related deaths, with a five-year survival rate of only 6 percent, she said.

The scientists found that apigenin inhibited an enzyme called glycogen synthase kinase-3? (GSK-3?), which led to a decrease in the production of anti-apoptotic genes in the pancreatic cancer cells. Apoptosis means that the cancer cell self-destructs because its DNA has been damaged.

In one of the cancer cell lines, the percentage of cells undergoing apoptosis went from 8.4 percent in cells that had not been treated with the flavonoid to 43.8 percent in cells that had been treated with a 50-micromolar dose. In this case, no chemotherapy drug had been added.

Treatment with the flavonoid also modified gene expression. "Certain genes associated with pro-inflammatory cytokines were highly upregulated," de Mejia said.

According to Johnson, the scientists' in vitro study in *Molecular Nutrition and Food Research* is the first to show that apigenin treatment can lead to an increase in interleukin 17s in pancreatic cells, showing its potential relevance in anti-pancreatic cancer activity.

Pancreatic cancer patients would probably not be able to eat enough flavonoid-rich foods to raise blood plasma levels of the flavonoid to an effective level. But scientists could design drugs that would achieve those concentrations, de Mejia said.

And prevention of this frightening disease is another story. "If you eat a

lot of fruits and vegetables throughout your life, you'll have chronic exposure to these bioactive flavonoids, which would certainly help to reduce the risk of cancer," she noted.

More information: Flavonoid apigenin modified gene expression associated with inflammation and cancer and induced apoptosis in human pancreatic cancer cells through inhibition of GSK-3?/NF-?B signaling cascade is available pre-publication online in *Molecular Nutrition and Food Research* at onlinelibrary.wiley.com/doi/10 … 2/mnfr.201300307/pdf.

Interactions between dietary flavonoids apigenin or luteolin and chemotherapeutic drugs to potentiate anti-proliferative effect on human pancreatic cancer cells in vitro is available pre-publication online in *Food and Chemical Toxicology* at ac.els-cdn.com/S02786915130049 … 91513004912-main.pdf

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