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Antioxidants in Diabetic Meds Fuel Cancer Wildfire

By Lila Abassi — April 15, 2016

Antioxidants via Shutterstock [1]

Antioxidants [2] are either manmade or natural substances that have been found to protect cells from damage due to reactive oxygen species (ROS) – highly reactive and toxic molecules that are formed as a natural byproduct of oxygen metabolism and, in excess, are referred to as oxidative stress – a condition of imbalance between antioxidants and ROS.

We have all heard the benefits of consuming foods that contain antioxidants, however, there is mounting evidence [3] that these substances, when taken as supplements, are not the disease fighting powerhouses they were thought to be. In fact, studies have shown that taking large amounts of vitamin E, for example, not only *don't* help in prostate cancer prevention but may actually *increase* the risk and similar findings have been uncovered between beta carotene and lung cancer.

According to Colleen Doyle, MS, RD, Director of Nutrition and Physical Activity at the American Cancer Society, we must distinguish between supplements containing antioxidants and the foods that they come from.

"A number of trials which gave high-dose beta carotene supplements to people at high risk for lung cancer were actually stopped early because those people were developing lung cancer at higher rates, " she said. "Foods rich in beta carotene may be helpful in reducing the risk of lung cancer, but much research on beta carotene supplements suggest quite the opposite, at least for subgroups of the population."

A new study [4], published in *Science Translational Medicine*, found that in mice with cancer, common classes of drugs used to treat type 2 diabetes (T2DM) – dipeptidyl peptidase-4 inhibitors (DPP-4i) that include the drugs sitagliptin and saxagliptin, as well as alpha-lipoic acid (ALA), which aid in lowering blood sugar levels as well as relieving peripheral neuropathy – increased the spread of existing tumors.

The authors write that these medications stimulate the prolonged activation of nuclear factor E2-related factor 2 (NRF2), a signaling pathway which ultimately results in increased expression of

antioxidants and metastasis-promoting proteins as well as increased cancer cell migration. When the NRF2 gene was deactivated in mice with cancer, there was a subsequent mitigation of tumor metastasis caused by endogenous (naturally occurring) and DPP-4i antioxidants. When observing samples of human liver cancer tissue, scientists similarly found that activation of the NRF2 pathway by antioxidants was positively correlated with metastasis.

Type 2 diabetes (T2DM) itself, is a pathological condition promoting oxidative stress [5] in which the complications may include stroke, neuropathy, retinopathy and nephropathy. Accumulating evidence has linked [6] diabetes, insulin resistance and elevated insulin levels to increased risk of certain cancers. The common denominator of hyperinsulinemia, T2DM and cancer is elevated body fat. Body fat, in itself, has been strongly associated with several cancers such as pancreatic and colorectal cancer.

While medications such as DPP-4i and ALA, through their antioxidant effects, help to attenuate diabetes symptoms, in the setting of an existing cancer, they may cause significant problems. It will be imperative that these drugs be used cautiously in diabetic patients with cancer. Additionally, there may be value in targeting the NRF2 signaling pathway for therapeutic intervention to halt the metastatic spread of tumors.
