Oxidative Stress in Relation to the Use of Specialty Dietary Supplements

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Oxidative stress is thought to play a role in the development of cancer, heart disease, and many other chronic diseases. In general, the body has the ability to prevent and repair the cell damage caused by reactive oxygen species. However, when this capability is overwhelmed, oxidative stress occurs, resulting in damage to DNA and other cell components. Some vitamin and mineral supplements, such as Vitamin C, Vitamin E and selenium, are thought to have an antioxidant effect. This is of great interest because of its potential for disease prevention. However, little is known about the effects of specialty (non-vitamin, non-mineral) supplements, such as glucosamine, chondroitin, ginseng, and garlic, on oxidative stress and DNA damage and repair.

Drs. Elizabeth Kantor, Emily White, Cornelia Ulrich and colleagues in PHS, CRD, and the German Cancer Research Center in Heidelberg investigated the associations between oxidative stress, DNA damage and repair, and ten specialty supplements thought to have anti-inflammatory or antioxidant effects. 209 subjects from the VITamins And Lifestyle (VITAL) biomarker study were included, and they were interviewed about their use of glucosamine, chondroitin, fish oil, coenzyme Q10 (CoQ10), methylsulfonylmethane (MSM), garlic, ginseng, ginkgo, saw palmetto, and fiber. Subjects also provided blood and urine samples, which were used to estimate oxidative stress and DNA damage and repair capacity. Two biomarkers of oxidative stress were measured in urine, including 8-isoprostane and PGF2-α, and both were corrected for levels of urinary creatinine. DNA damage was estimated using the Comet assay, a single cell measurement of DNA double strand breaks, and DNA repair capacity was evaluated at 15 and 60 minutes after irradiation of viable lymphocytes.

After accounting for differences in potential confounding factors, none of the specialty supplements were associated with levels of 8-isoprostane. People who had reported taking at least 14 glucosamine pills per week had 40% lower levels of PGF2-α, the other measure of oxidative stress, compared to non-users (p-value for trend: 0.01). Similarly, use of chondroitin (at least 14 pills per week) was associated with 47% lower PGF2-α compared to non-users (p-value for trend: 0.003). Since all chondroitin users were also taking glucosamine, investigators looked for an association among the 19 subjects using glucosamine alone, and observed no association. Dr. Kantor and co-

authors pointed out that this may be due to the smaller sample size (and thus limited statistical power) in this analysis, or it may be that chondroitin alone is responsible for the observed association. It may also be that glucosamine and chondroitin act in concert; biologic studies provide some evidence for this. PGF2-α concentrations were also 43% lower among people who reported using at least 1 fiber supplement per week during the previous month (p-value: 0.01). This is consistent with some prior studies showing antioxidant effects of fiber in humans, but in those studies the fiber was taken in combination with other dietary factors, and so it was difficult to assess the role of fiber alone.

In terms of DNA damage and repair, use of CoQ10 was the only supplement associated with baseline DNA damage (58% lower among users versus non-users; p-value: 0.003). Past studies investigating the effects of CoQ10 on DNA damage have been sparse and have had mixed results. No supplements were associated with DNA repair capacity at 15 minutes after irradiation. One supplement, MSM, was associated with *decreased* repair capacity at 60 minutes post-irradiation (47% vs 64% of induced damage was repaired at 60 minutes in users versus non-users of MSM), even though *in vitro* studies have suggested that MSM reduces oxidative stress. Further studies will be necessary to confirm or refute these associations.

"This research is exciting, as it is the first human study to suggest that glucosamine and chondroitin use is associated with reduced oxidative stress," Dr. Kantor noted. This is consistent with *in vitro* and animal studies which have suggested that these supplements may reduce oxidative stress. Furthermore, the use of glucosamine and chondroitin have been linked to a lower risk of colorectal and lung cancers, and so this study provides a possible biologic mechanism for this association. However, Dr. Kantor acknowledged that more research is needed, "to better understand these associations and the chemopreventive potential of these supplements."

Kantor ED, Ulrich CM, Owen RW, Schmezer P, Neuhouser ML, Lampe JW, Peters U, Shen DD, Vaughan TL, White E. 2013. Specialty supplement use and biologic measures of oxidative stress and DNA damage. Cancer Epidemiol Biomarkers Prev. Aug 5. [Epub ahead of print]