

S-VI-1

CHLOROPHYLLIN REDUCES URINARY LEVELS OF A CARCINOGEN-DNA ADDUCT BIOMARKER IN A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Patricia Egner^a, Jin-Bing Wang^b, Yuan-Rong Zhu^b, Bao-Chu Zhang^b, Yan Wu^b, Qi-Nan Zhang^b, Geng-Sun Qian^c, Shuang-Yuan Kuang^c, Stephen Gange^a, Lisa Jacobson^a, Kathy Helzlsouer^a, George Bailey^d, John Groopman^a, and Thomas Kensler^a

^aJohns Hopkins University Bloomberg School of Public Health, Baltimore, MD, USA; ^bQidong Liver Cancer Institute, Qidong, Jiangsu Province, P.R. China; ^cShanghai Cancer Institute, Shanghai, P.R. China; ^dOregon State University, Corvallis, OR, USA
E-mail: tkensler@jhsph.edu

Residents of Qidong, Peoples Republic of China, are at high risk for development of hepatocellular carcinoma, in part due to consumption of foods contaminated with aflatoxins. Chlorophyllin, a mixture of semi-synthetic, water-soluble derivatives of chlorophyll that is used as a food colorant and over-the-counter medicine, has been shown to be an effective inhibitor of aflatoxin hepatocarcinogenesis in animal models. Chlorophyllin may act through formation of complexes with aromatic rings in carcinogens, thereby blocking bioavailability. In a randomized, double-blind, placebo-controlled chemoprevention trial, we tested whether chlorophyllin could alter the disposition of aflatoxin. One hundred eighty healthy adults from Qidong were randomly assigned to ingest 100 mg chlorophyllin or a placebo three times a day for four months. The primary endpoint was modulation of levels of aflatoxin-N⁷-guanine adducts in urine samples collected three months into the intervention measured using sequential immunoaffinity chromatography and liquid chromatography-electrospray mass spectrometry. This aflatoxin-DNA adduct excretion product serves as a biomarker of the biologically effective dose of aflatoxin and elevated levels are associated with increased risk of liver cancer. Adherence to the study protocol was outstanding as only one person dropped out. Overall, 97% of the tablets were consumed during the study. No adverse events were reported.

Aflatoxin-N⁷-guanine could be detected in 105 out of 169 available samples. Chlorophyllin consumption at each meal led to an overall 55% reduction ($p = 0.036$) in median urinary levels of this aflatoxin biomarker compared to those taking placebo. Among participants with detectable levels of the DNA damage biomarker, the geometric mean level for the chlorophyllin arm (0.18 pg/mg creatinine) represented a highly significant ($p < 0.001$) 49% reduction compared to that of the placebo arm (0.35 pg/mg creatinine). Chlorophyllin proved to be a safe and effective agent for reducing aflatoxin-DNA adduct formation in individuals consuming dietary aflatoxins. Prophylactic interventions with chlorophyllin or supplementation of diets with foods rich in chlorophylls may represent practical means to prevent the development of hepatocellular carcinoma or other environmentally-induced cancers.