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SHORT COMMUNICATION

Reduction of oxidative DNA-damage in humans by Brussels sprouts

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The effect of consumption of Brussels sprouts on levels of 8-oxo-7,8-dihydro-2′-deoxyguanosine (8-oxodG) in human urine was investigated in 10 healthy, male, non-smoking volunteers. Following a 3 week run-in period, five volunteers continued on a diet free of cruciferous vegetables for a subsequent 3 week intervention period (control group), while the other five (sprouts group) consumed 300 g of cooked Brussels sprouts per day, at the expense of 300 g of a glucosinolate-free vegetable. Levels of 8-oxodG in 24 h urine samples were measured by HPLC. In the control group there was no difference between the two periods in levels of 8-oxodG (P = 0.72). In contrast, in the sprouts group the levels of 8-oxodG were decreased by 28% during the intervention period (P = 0.039). The present findings support the results of epidemiologic studies that consumption of cruciferous vegetables may result in a decreased cancer risk.

The cancer-preventing potential of naturally occurring substances in the diet is a main area of scientific interest (1). Many foods (fruits and vegetables like cabbage, leeks, citrus, herbs and spices) and food ingredients (e.g. antioxidant vitamins, flavonoids, glucosinolates, organosulfur compounds) have been claimed to have antimutagenic or anticarcinogenic potential. Most of these claims are based on results obtained in short-term mutagenicity tests *in vitro* and/or experiments with animals. However, the definite proof whether or not the experimentally observed antimutagenic or anticarcinogenic effect is also feasible in humans under normal dietary conditions can only come from studies with humans (2). As such, epidemiological studies indicate that fruit and vegetable intake is inversely associated with the risk of cancer (3,4). In particular cruciferous vegetables like cabbage, Brussels sprouts and broccoli have been attributed beneficial health effects in humans (5). However, there are also experimental data showing that certain indoles and isothiocyanates, breakdown products of glucosinolates, are tumour promotors and are genotoxic (6). Oxidative DNA damage is considered a pathogenic event in many cancers (7–9). Thus a reduction in the rate of oxidative DNA damage may indicate a reduced risk of cancer. The most abundant and potentially mutagenic lesion induced in DNA by reactive oxygen species is 8-oxo-7,8-dihydro-2′-deoxyguanosine (8-oxodG*) (9). *In vivo* this DNA adduct is repaired by excision and the resulting product, 8-oxodG, is excreted unchanged and independently of diet into the urine (10). The rate of this excretion thus serves as a biomarker of the integrated rate of oxidative DNA damage in the whole body (10,11).

We have investigated the hypothesis that the beneficial effects of cruciferous vegetables in humans are due to antioxidant properties that result in a reduction in oxidative DNA damage. Ten healthy male non-smoking volunteers were randomly allocated to a control group and a (Brussels) sprouts group after giving their informed consent. The volunteers refrained from any cruciferous vegetables and consumed 300 g of cooked non-cruciferous vegetables, e.g. endives, French beans, peas, beets, macédoine (mixed legumes and vegetables), fava beans and chicory, per day for a period of 3 weeks. During a subsequent 3 week intervention period the five subjects from the control group continued the non-cruciferous vegetable intake, whereas the five subjects from the sprouts group changed to the consumption of 300 g of cooked Brussels sprouts per day. This is the same intervention study as reported on previously (12). On experimental days 12 and 33 (i.e. near the end of weeks 2 and 5) urine was collected for a period of 24 h. The concentration of 8-oxodG was measured by HPLC as previously described (11). The two samples from each subject were assayed together at least twice in separate runs and the average values used for data analysis. Quantification was accomplished by establishing three-point calibration curves for each sample by addition of genuine compound.

The consumption of Brussels sprouts was not associated with any adverse effects as apparent from vital signs and a variety of clinico-chemical parameters for liver, renal, thyroid and blood-coagulation functions (data not shown).

The 8-oxodG excretion in 24-h urine was not significantly

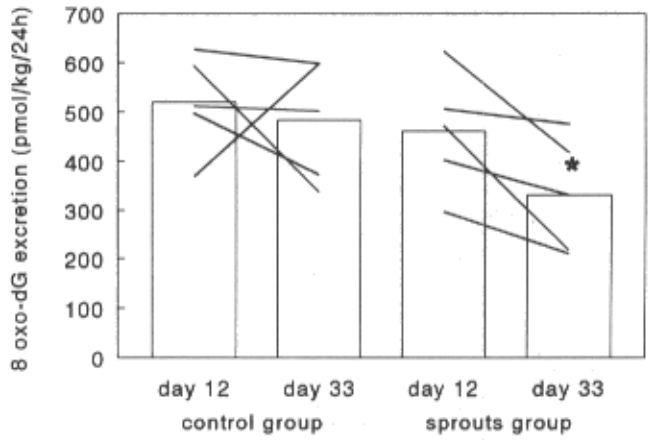

Fig. 1. Levels of 8oxo-dG in urine (pmol/kg/24 h) in the control group and the sprouts group on experimental day 12 (i.e. the control period in which no cruciferous vegetables were consumed) and on experimental day 33 (i.e. during the intervention period when the sprouts group consumed 300 g of cooked Brussels sprouts at the expense of 300 g cooked non-cruciferous vegetables). Asterisk denotes within-group differences at P = 0.039 versus experimental day 12. Mean group values and individual data.

***Abbreviation:** 8-oxodG, 8-oxo-7,8-dihydro-2′-deoxyguanosine.

different between the control and the sprouts group during the initial period (Figure 1). Within the control group there was no significant difference in 8-oxodG excretion between the two periods; a nominal 5% decrease (−46% to 35%; 95% confidence interval) was seen ($P = 0.72$). In contrast, within the sprouts group, the excretion of 8-oxodG decreased by 28% (-54% to -2%; 95% confidence interval) during the intervention ($P = 0.039$, paired t-test). In the intervention period, the 8-oxodG excretion was 29% (-70% to 12%; 95% confidence interval) lower in the sprouts group than in the control group after adjustment for differences in the initial values ($P = 0.14$ by analysis of covariance). It is noted that the 8-oxodG excretion was higher in the present young, lean male subjects than in our previously reported results in women and older subjects of both sexes and a broad weight range: the factors male sex, leaness and young age (and smoking) are important determinants conveying a high 8-oxodG excretion (11,13).

The present data suggest that Brussels sprouts have putative antimutagenic and anticarcinogenic properties by decreasing the rate of oxidative damage to DNA. This is in line with recent findings that some glucosinolates (though not extracts of Brussels sprouts) prevent peroxidation of human microsomes *in vitro* (14). This lends further support to the notion that cruciferous vegetables have health-promoting effects under physiologically feasible conditions and without apparent side effects (2). In general, the beneficial effects of vegetables have been related to their content of antioxidant vitamins, such as vitamin C and β-carotene, as well as other antioxidants. However, cruciferous vegetables differ in particular from other vegetables by the presence of glucosinolates. Thus, the apparently specific reducing effect of Brussels sprouts on oxidative DNA damage may seem to be attributable to one or more of these phytochemicals. We have previously demonstrated an induction of the detoxification enzyme glutathione-S-transferase α in the same study (12). The present results indicate a possible second pathway for the cancer-preventing capacity of phytochemicals in cruciferous vegetables. The use of 8-oxodG as a biomarker for oxidative damage can allow determination of dose−effect relationships with vegetable intake and identification of the preventive principle(s) of Brussels sprouts and possibly other vegetables. Further research to confirm and expand the present findings is warranted.

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