

# A HUMAN INTERVENTION TRIAL FOR IDENTIFICATION OF THE CHEMOPREVENTIVE PROPERTIES OF ISOTHIOCYANATES (ITCS) IN MUSTARD

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**Background:** Chemopreventive constituents in food plants such as Brassica-derived isothiocyanates <ITCs> have been shown to be quite effective in the prevention of genotoxic DNA damage in cell culture models < and >. carcinogenesis in laboratory animals. Additionally, human intervention trials with Brassica vegetables have been conducted to determine the bioavailability of ITCs from these plants or to investigate the modulation of carcinogen detoxifying enzymes involved in xenobiotic metabolism in blood of volunteers. Mustard <sinapis alba> contains ITCs at very high concentrations; however, so far, no information is available on the chemopreventive potency of mustard preparations in humans.

**Study design:** Our group conducted a human intervention trial to investigate the effect of mustard intake on *ex vivo* induced DNA damage. The study was conducted with the approval of the ethics committee of the University of Freiburg < and >.with the informed consent of the participants. First, we carried out a study with 6 human volunteers to investigate the time dependent effect of mustard intake on DNA damage induced by hydrogen peroxide and benzo<a>pyrene diole epoxide <BPDE> in leucocytes. In a follow-up study with 14 human volunteers we further tested the quality of the DNA protective effect by the use of detecting micronucleus induction additionally to DNA strand break formation.

**Material and Methods:** For both trials, human volunteers were fed twenty g of mustard preparation daily for four days. One week before intervention until one week post intervention, participants followed a controlled diet to minimize the influence of other bioactive compounds. Before intervention begin < and >. subsequent every twelve h <in the 1st intervention trial> or after 72 h < in the 2nd trial> heparinized blood was collected by venipuncture. Whole blood was immediately exposed to the genotoxins < and >.subsequently processed for the detection of DNA strand breaks in the comet assay. For the micronucleus test, lymphocytes were isolated from participants' blood by density gradient centrifugation and stimulated for proliferation with phytohaemagglutinin <PHA> before additional treatment with cytochalasin B. Lymphocyte exposure to the genotoxins was done 44 h after cultivation begin.

**Results and Conclusion:** Our results clearly show that a significant protection of human leucocytes from DNA damage induced by both toxins was achieved by mustard intake already 12 h post intervention begin as assessed by the comet assay. Furthermore, the induction of micronuclei by hydrogen peroxide or BPDE in isolated human lymphocytes could be significantly inhibited by mustard ingestion. The results show that intake of ITC-containing vegetables might indeed be associated with reduced cancer risk through a reduction in DNA damage.