



Cancer prevention through dietary compounds – a novel approach using fish models

Issue & Goal of Research

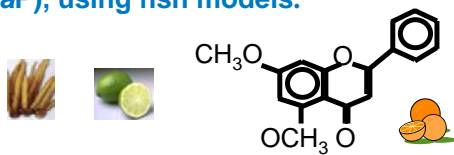


Carcinogens, such as polycyclic aromatic hydrocarbons (PAHs), are abundant in exhaust, tobacco smoke and our diet, and have been implicated in cancers of the aerodigestive tract in humans (e.g., lung cancer).

The same carcinogens are abundant in the marine environment. Many fishes exhibit susceptibility to liver cancer.



It is the goal of this research project to investigate the chemopreventive potential and mechanism of the dietary flavonoid 5,7-dimethoxyflavone (DMF) in inhibiting adverse biological effects exerted by environmental pollutants, such as the PAH Benzo[a]pyrene (BaP), using fish models.

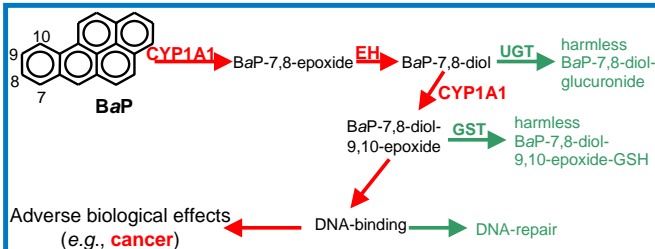


5,7-Dimethoxyflavone (DMF)

Scientific Approach

Objective 1 – To determine the protective properties of DMF on DNA-binding of BaP as well as on BaP-bioactivating and BaP-bioinactivating enzymes *in vitro* in cultured fish hepatocytes.

Objective 2 – To determine the protective properties of DMF on DNA-binding of BaP, as well as on BaP-bioactivating and -bioinactivating enzymes in the fish after *in vivo* DMF-exposure.



Previous findings have shown:

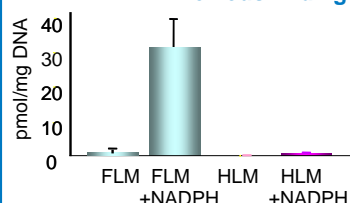


Fig. 1. DNA-adduct formation of 1 μM ³H-BaP using *Fundulus* Liver Microsomes (FLM) and calf thymus DNA significantly exceeded (MW-U, p = 0.002) that of Human Liver Microsomes (HLM) by about 45-fold.

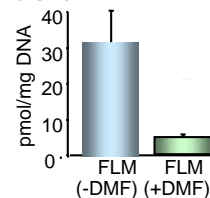


Fig. 2. DNA-binding of BaP to calf thymus DNA using *Fundulus* Liver Microsomes was significantly inhibited by co-incubating with 25 μM DMF (ANOVA, p < 0.001).

Preliminary Results

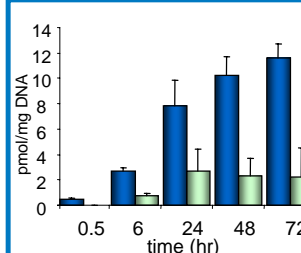


Fig. 3. Binding of ³H-BaP to DNA in cultured trout hepatocytes treated with 1 μM BaP increased significantly over 24 - 72 hours (p < 0.01, ANOVA), but was dramatically inhibited when co-incubated with 25 μM DMF.

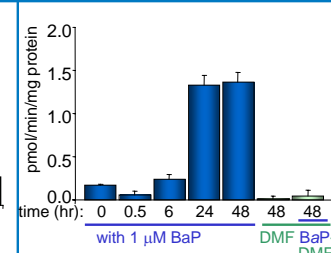


Fig. 4. Catalytic activity of CYP1A in cultured trout hepatocytes treated with 1 μM BaP increased significantly over 24-48 hours, but was dramatically inhibited when co-incubated with 25 μM DMF or with DMF alone.

Preliminary Conclusions & Impact

The dietary flavonoid 5,7-Dimethoxyflavone seems to be a potent inhibitor of the bioactivation of BaP and subsequently binding of this carcinogen to DNA, as shown *in vitro* as well with cultured trout hepatocytes. Fish & mammals respond similarly to many pollutants on a biochemical level. Using sensitive fish models may provide an efficient and unique angle to elucidate pathways of chemical carcinogenesis, and a potential prevention technique that may contribute to the increase in quality and years of healthy life in humans.