US EPA ARCHIVE DOCUMENT

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004 EPA STAR Graduate Fellowship Conference *Next Generation Scientists—Next Opportunities*

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

sue & Goal of Research

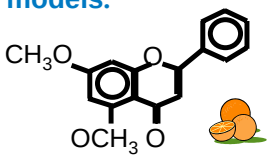


arcinogens, such as polycyclic aromatic ydrocarbons (PAHs), are abundant in exhaust, bacco smoke and our diet, and have been plicated in cancers of the aerodigestive tract in mans (*e.g.*, lung cancer).

e same carcinogens are abundant in the arine environment. Many fishes hibit susceptibility to liver cancer.

is the goal of this research project to vestigate the chemopreventive potential and echanism of the dietary flavonoid 5,7-methoxyflavone (DMF) in inhibiting adverse ological effects exerted by environmental llutants, such as the PAH Benzo[*a*]pyrene *a*P), using fish models.



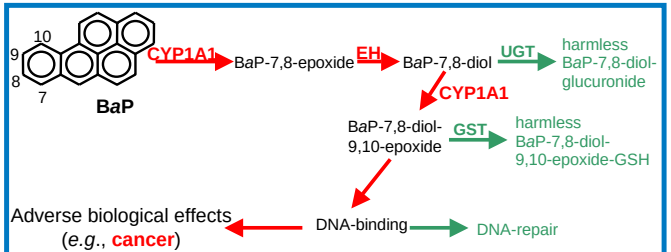


5,7-Dimethoxyflavone (DMF)

Scientific Approach

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

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



Previous findings have shown:

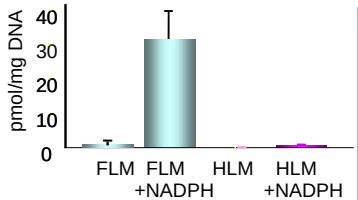


Fig. 1. DNA-adduct formation of 1 µM ^{3}H-BaP using *Fundulus* Liver Microsomes (FLM) and calf thymus DNA significantly exceeded (MW-U, p = 0.002) that of Human Liver Microsomes (HLM) by about **45-fold**.

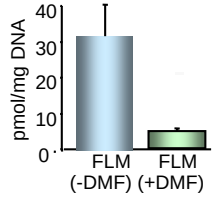


Fig. 2. DNA-binding of BaP to calf thymus DNA using *Fundulus* Liver Microsomes was significantly **inhibited by co-incubating with 25 µM DMF** (ANOVA, p < 0.001).

Preliminary Results

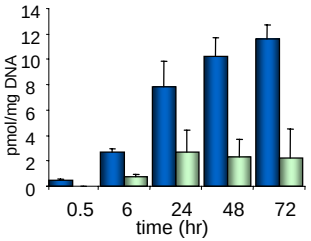


Fig. 3. Binding of ^{3}H-BaP to DNA in cultured trout hepatocytes treated with 1µM BaP increased significantly over 24 - 72 hours (p<0.01, ANOVA), but was dramatically inhibited when co-incubated with 25 µM DMF.

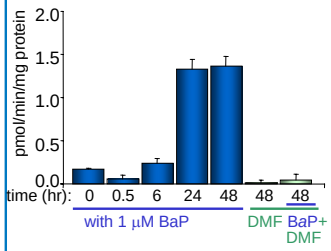


Fig. 4. Catalytic activity of CYP1A in cultured trout hepatocytes treated with 1µM BaP increased significantly over 24-48 hours, but was dramatically inhibited when co-incubated with 25 µM DMF or with DMF alone.

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.

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