Mechanisms by which fruit polyphenols act as cancer chemopreventive agents





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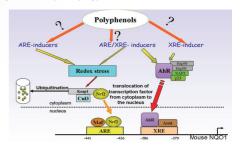
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Introduction

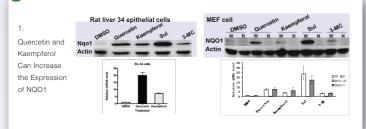
Regular consumption of fruit and vegetables correlates with a decreased incidence of cancer. Polyphenols are thought to contribute to this and their chemopreventive effect may relate to their ability to induce genes for antioxidant and detoxification enzymes, such as NAD(P)H:quinone oxidoreductase (NQO1), possibly through the antioxidant response element (ARE) and/or the xenobiotic response element (XRE). Our study has examined the mechanisms putatively responsible for a polyphenol-derived cancer chemoprevention effect with specific focus on Nrf2, a redox-sensitive transcription factor and CYP1A1, a member of the cytochrome P450 superfamily, known to operate as an arylhydrocarbon hydroxylase. The flavonols quercetin and kaempferol were used as model polyphenols for our studies.

Hypothesis

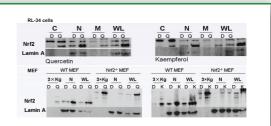
At what point in the body's antioxidant and detoxification systems do plant polyphenols exert there action, if at all?



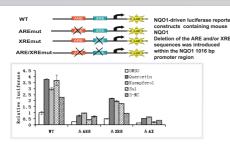
Experimental Approach and Results



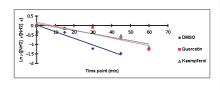
Quercetin and Kaempferol alte the intracellular localization of Nrf2.



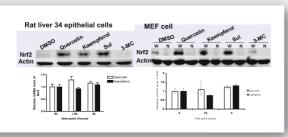
The Involvement of ARE and XRE in the Induction of NQO1 by Quercetin and Kaempferol.



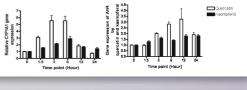
carried out in the presence and Kaempferol to showing both chemicals can increase the half life of Nrf2 protein in RI 34 cells



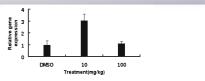
Quercetin and Kaempferol car increase the expression of protein level but have no effect on the mRNA



Quercetin and Kaempferol increase mRNAs of



expression of CYP1A1 in mouse small intestine



Conclusion

Quercetin and Kaempferol can increase the expression of antioxidant and detoxification enzymes NQO1 and CYP1A1.

The induction of NQO1 is dependent on ARE and partially on XRE.

Induction is regulated by Nrf2 which can be stabilized by Quercetin and Kaempferol.

Furthermore, intervention studies with mice using Quercetin at 10mg/kg for 4 days saw an associated increase in CYP1A1 mRNA level in the mouse's small intestine perhaps suggesting positive benefits with regard to risk of digestive tract cancers