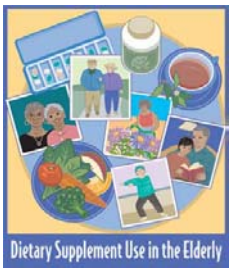

Polypharmacy and OTCs: What Is the Impact of Dietary Supplements on Gene Networks That Regulate Drug Clearance?

Barry Marc Forman, M.D., Ph.D.

Beckman Research Institute, Duarte, CA

Human beings are constantly exposed to potentially toxic chemicals present in food, drugs, and the environment. We also are challenged by toxic by-products of chemical reactions within our own bodies. These toxins need to be inactivated and/or excreted to maintain homeostasis. Pregnane X Receptor (PXR), is a promiscuous nuclear receptor that is expressed in the liver and intestine and is activated by a diverse array of endogenous and exogenous compounds (e.g., taxol, rifampicin, St. John's Wort, etc.) Upon activation, PXR coordinately regulates a number of genes involved in drug clearance via the liver (Cytochrome P450s) and intestine (P-glycoprotein). Although this pathway has evolved as a protective mechanism, it also facilitates drug-drug interactions that can eliminate therapeutic activity. In this presentation, we review the data underlying this phenomenon and discuss how dietary supplements can induce these transcriptional pathways and thus limit the therapeutic potential of co-administered drugs. Our findings suggest that common dietary supplements may activate PXR and thus promote unwanted interactions between dietary supplements and pharmaceutical agents. To promote the safe use of dietary supplements, we suggest that all commercially available supplements be routinely tested for their ability to activate PXR-mediated drug clearance.

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