How Do Interactions Between Prescription Drugs and Botanical Dietary Supplements Have Potential to Harm Us?

Steven Kliewer, Ph.D.
Departments of Molecular Biology and Pharmacology
University of Texas Southwestern Medical Center
Dallas, TX
Drug-Drug Interactions

- Occur when one drug interferes with the actions of a second drug, sometimes with life-threatening consequences
- Growing problem in US since
  - 7% of population take 5 drugs or more
  - In women ≥65 yrs, 25% take 5 drugs or more
- Problem complicated by herbs/supplements
  - 16% of those taking prescription drugs also use herbs/supplements

Source of statistics: JAMA 287: 337
**PXR Causes Drug-Drug Interactions**

**Drug #1**
- rifampicin
- taxol
- phenobarbital
- St. John’s wort

**PXR receptor**

**Drug metabolism genes**

**Metabolism of Drug #2**
- cyclosporin
- indinavir
- gleevec
- simvastatin
St. John’s Wort Interacts with Drugs

- Unregulated medicinal herb
- Widely used for depression
  - European sales of $6 billion (1998)
- Interacts with drugs
  - cyclosporin
  - indinavir
  - gleevec
  - simvastatin

SJW-drug interactions can be life threatening
St. John’s Wort Activates PXR

Cell-based assay

SJW is predicted to interact with many drugs
St. John’s Wort Interacts with Drugs

cyclosporin................immunosuppressant nevirapine............antiviral
tacrolimus................immunosuppressant indinavir...............antiviral
quazepam...................sedative irinotecan.........antineoplastic
warfarin...................anticoagulant gleevec...............antineoplastic
verapamil..................antihypertensive amitriptyline....antidepressant
nifedipine..................antihypertensive simvastatin.......anticholesterolemic
omeprazole..............antiulcerative digoxin.................cardiotonic
theophylline.............bronchodilator methadone..........analgesic
ethinylestradiol.......oral contraceptive alprazolam.........anxiolytic
midazolam.................anesthetic

Many of these interactions can be life threatening

Do other herbs activate PXR?
Gugulipid Activates PXR

- Derived from mukul myrrh tree
- Promoted for reducing cholesterol and treating obesity
- Accelerates the metabolism of two antihypertension drugs
  - diltiazem
  - propranolol

Gugulipid may counteract other drugs including statins
Hops Activates PXR

• Promoted for treating
  - insomnia
  - anxiety
  - indigestion
• Increases drug metabolizing enzymes in rodents

Hops is predicted to interact with most drugs
Herbs Activate PXR

St. John’s wort

gugulipid

hops

others?

>50% of drugs

Drug metabolism

genes

Drug metabolism
PXR Assays Predict Herb-Drug Interactions

- Reliable
- Efficient

Herb-drug interactions can be predicted and prevented
Summary

• Activation of PXR causes harmful drug-drug interactions
• Unregulated herbs activate PXR
  – St. John’s wort
  – gugulipid
  – hops
  – others?
• PXR assays can be used to predict herb-drug interactions
• A commitment should be made to assess and to disclose the risks of dietary supplements
• This commitment should include additional funding for basic and clinical research into dietary supplements