SAFETY WITH DRUGS,
AVOID ERRORS

Sponsorships:

Italian Society of General Practice, Active Citizenship
Award “Renato Grandene 2017 for technological innovations
Federation of Italian Pharmacists Associations
Two-thirds of patients with at least 4 medications are exposed to the risk of adverse events from interactions.

In the USA interactions cause almost 4 percent of all emergency room accesses and about a third of all adverse events in hospitalized patients.

A STRONG SCIENTIFIC BASIS

✓ over 4.500 drug monographs
✓ over 12.000 active principles
✓ over 9.000 values of the ratio between the concentrations in the studies of pairs
✓ over 20.000 induction or inhibition constants
✓ over 8000 clinical trials

Developed in collaboration with the University of Modena and Reggio Emilia (ITA), continuously updated

INNOVATION

✓ NOT ONLY DRUGS, but also herbal products, supplements, drugs of abuse, foods, etc..
✓ NOT ONLY PAIRS: more than two active principles can create complex metabolic effects: if you take in account interactions only at the pairs level, you can fall into very serious mistakes. It is possible to check up to 30 active principles in your analysis.
✓ PROGRESSIVE LEVELS OF ANALYSIS: multiple tools, from the simplest to the most sophisticated, may support the development of a professional growth on this field
EASE OF USE

✓ Extensive use of intuitive graphical interfaces
✓ High consultation speed
✓ Search fields with automatic completion
✓ Tooltips for a better understanding of the text
✓ Possibility to use scientific names, brands, codes
✓ Online guide

CUSTOMIZATION

✓ Possibility to save your own analysis
✓ Possibility of in-depth analysis based on the client's characteristics
✓ Possibility to compose a letter to a physician, attaching graphics and customizing the text of the communication
✓ As the active principles are inserted, the list is composed and the correspondent textual part is quickly displayed

✓ Icons and underlined titles give access to a series of in-depth tools
ASSESS THE ALERTS IN AN APPROPRIATE WAY

✓ There are 4 risk levels, highlighted by an indicator that invites you to a gradual resolution of critical issues, from contra-indications to decreasing levels of caution.
✓ You may have an overview of the possible undesired effects of the chosen combination, divided by apparate, to better understand what is happening to your patient

✓ For many situations you’ll may find suggestions, from the scientific literature, on how to deal with any undesirable effects that require intervention
From tens of thousands of pharmacokinetic constants it is possible to reconstruct a scheme of how each active principle can interact with the various enzyme systems and transporters (over 300).
✓ It is possible to do an hypothesis on the variation of blood levels.

✓ It is clearly only an hypothesis built on enzymatic relationships and compared with their effects in “in vivo” studies, but without any guarantee of predictability.
✓ AVOID TO ADMINISTER TO THE PATIENT CONTRAINDICATED THERAPIES WITHOUT EVEN BEING AWARE OF THIS. A lot of criticalities are cryptic and impossible to remember, for example: "CONTRAINDICATED with CYP3A4 substrates that prolong QTc" or "AVOID with strong CYP2C9 inhibitors" or "NOT RECOMMENDED with ototoxic drugs". There are over 150 categories of this kind in the package inserts.

✓ IDENTIFY HIGHLY DANGEROUS SITUATIONS, also «quoad vitam»: only an overall view of pharmacokinetics, a peculiarity of this instrument, can allow it. Mere evaluation by pairs exposes to very serious errors, huge damages for the patient and heavy professional responsibilities.
AND OTHER TOOLS…

vs ATC NOGAD - Selective serotonin reuptake inhibitors (SSRI)

**bisoprolol vs citalopram**

**EXPECTED VARIATION OF BLOOD LEVELS**

- **Hypothesis:** Test against placebo for the first time.
- **Effect:** Test for the difference between two groups.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Loss of efficacy risk</th>
<th>Loss of safety risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram</td>
<td>0.10</td>
<td>0.01</td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>0.10</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**GFR previson**

**Patient data:**
- Creatinine = 2
- Age = 37
- Gender = Male
- Ethnicity = Afro American

**calculated GFR = 47.87**

(Equation CKD-EPI (70 years), equation S11 (>70 years))

Otherwise values only by age and gender

**calculate the expected variation of blood levels**

**AUC RATIO**

- **Loss of efficacy risk**
- **Loss of safety risk**
- **Toxicity risk**

**certainum modify auc of sulfasalazine:**

AUC rate = 3.225


**AUC RATIO**

Relationship between the concentration curves by couples:

- **warfarin -- amiodarone:**
  - Warfarin 2.108 (+110%) metabol.: s-warfarin (act. maint.)
  - Warfarin 2.001 (+100%) metabol.: r-warfarin (act. maint.)

- **amiodarone -- digoxin:**
  - Digoxin 1.6802 (+68.6%) metabol.: s-warfarin (act. maint.)

- **zolpidem -- ketosones:**
  - Zolpidem 1.7 (+70%)
…FOR THOSE WHO WANT TO DISCOVER THEM

**General Info**
CYP1A2 and CYP2D6 substrates. Caution in patients taking monoamine oxidase inhibitors. Caution is advised in using duloxetine with other SSRIs. Caution is advised in using duloxetine with tricyclic antidepressants.

**Lab test interactions**
No interaction or no data in the database.

**Interactions with food intake**
Food does not affect the bioavailability of duloxetine. It is absorbed from the gastrointestinal tract and distributed in the body. It is excreted via the urine.

**More common adverse events**
- Headache
- Tachycardia
- Decreased libido
- Nausea
- Dry mouth
- Constipation
- Insomnia
- Increased appetite
- Weight gain

**duloxetine**

**LETTER TO THE DOCTOR**

- Evidence of critical issues without symptoms reported by the patient. We point out to your attention for an appropriate evaluation.
- Evidence of critical issues with symptoms reported by the patient. We point out promptly to your attention for an appropriate action.
- Evidence of severe critical issues and contraindications. We point out promptly to your attention for an appropriate action.

**CRANBERRY WARFARIN**

The objective is to report a case of warfarin-cranberry juice interaction, which resulted in an international normalized ratio (INR) elevation on 2 separate occasions. A 45-year-old female was receiving a total weekly dose of 95 mg of warfarin. During the 4 months prior to the incident, her INR was 2.6, with a range of 2.4-2.7, while taking the same weekly dose of warfarin. Her INR increased to 4.6 after drinking approximately 1.9 quarts (1400 mL) of cranberry juice cocktail daily for 2 days. Her INR 14 days later without cranberry juice was 1.9, while taking 95 mg of warfarin and INR was 2.1. At a subsequent visit, after drinking approximately 2 quarts (1600 mL) of cranberry juice daily for 3 days, her INR had increased to 4.5. Her INR after holding warfarin for 3 days was 1.8. Her INR 7 days after resuming the weekly dose of cranberry juice was 2.5. During the 6 weeks of the elevated INR episodes, no other factors were identified that would have resulted in an elevated INR, such as drugs, food, disease, or other known interactions. An objective causality assessment revealed the interaction was highly probable. Everyone is most commonly used instead of warfarin for chronic therapy. There have been several case reports of cranberry juice or cranberries causing inhibition of warfarin by elevating the INR. However, these trials evaluating this interaction failed to demonstrate a significant effect on an INR. Our case report describes INR elevation in a patient previously stable on warfarin after ingestion of cranberry juice cocktail daily for several days. The increase occurred on 2 separate occasions, which corresponded but were from other published literature.


PUBLISHED

This case report on a patient whose International Normalized Ratio (INR) increased after ingestion of cranberry juice while stabilized on warfarin. It is followed by a review of the published literature on the potential interaction between the two. An 85-year-old woman with chronic warfarin therapy for atrial fibrillation experienced INR elevations off to these factors after two separate ingestions of cranberry juice. In each case, her INR values decreased after eliminating one or two factors and not resuming a similar maintenance dose of warfarin. Although the majority of the pharmacokinetics and pharmacodynamic studies did not find a significant interaction between cranberry and warfarin, several case reports indicate that cranberry consumption can increase INR values in patients on warfarin. Physicians should consider cranberry usage as a potential contributor to the evaluation of supratherapeutic INR values in patients on warfarin.

Cranberry Warfarin: A Case Report and Review of the Literature. Hemann DL, Cauthen VA, Barney EC.

PUBLISHED