INTERACTIONS EXPLORER

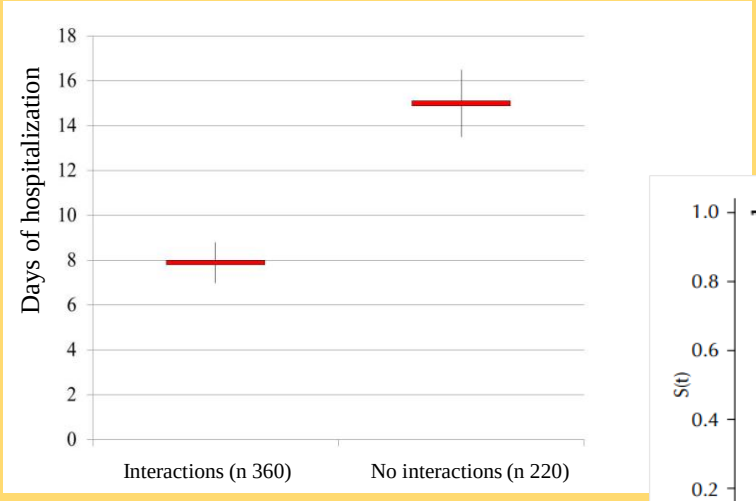
SAFETY WITH DRUGS, AVOID ERRORS

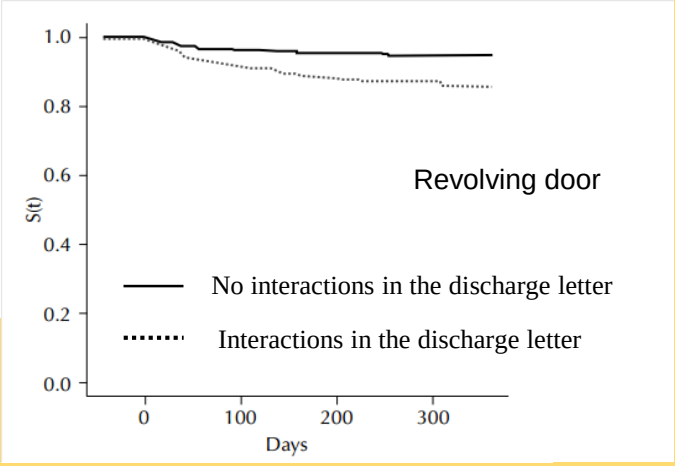
Sponsorships:

Italian Society of General Practice, Active Citizenship
Award “Renato Grandene 2017 for technological innovations
Federation of Italian Pharmacists Associations

INTERACTIONS: SILENT EPIDEMIC

- ✓ 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





Gagne et al. 2008; National Academies of Science - NAS -. 2005; Moura et al. 2009, 2012

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

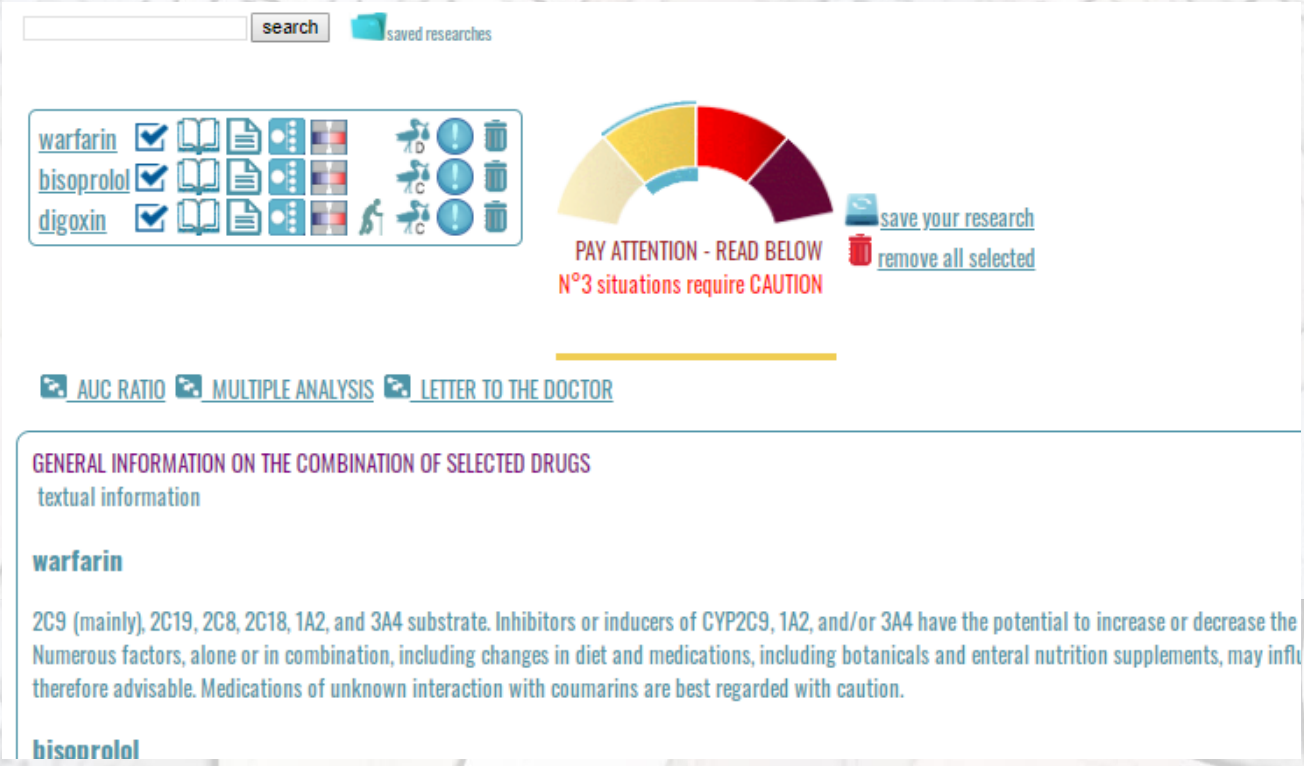
CUSTOMIZATION

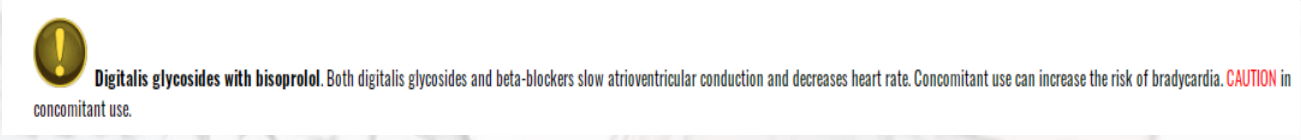
- ✓ Possibility to save your own analysis
- ✓ Possibility of in-depth analysis based on the client's characteristics
- ✓ Possibility to compose a letter to a physician, attaching graphics and customizing the text of the communication

SETTLE YOUR QUERY

- ✓ 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.

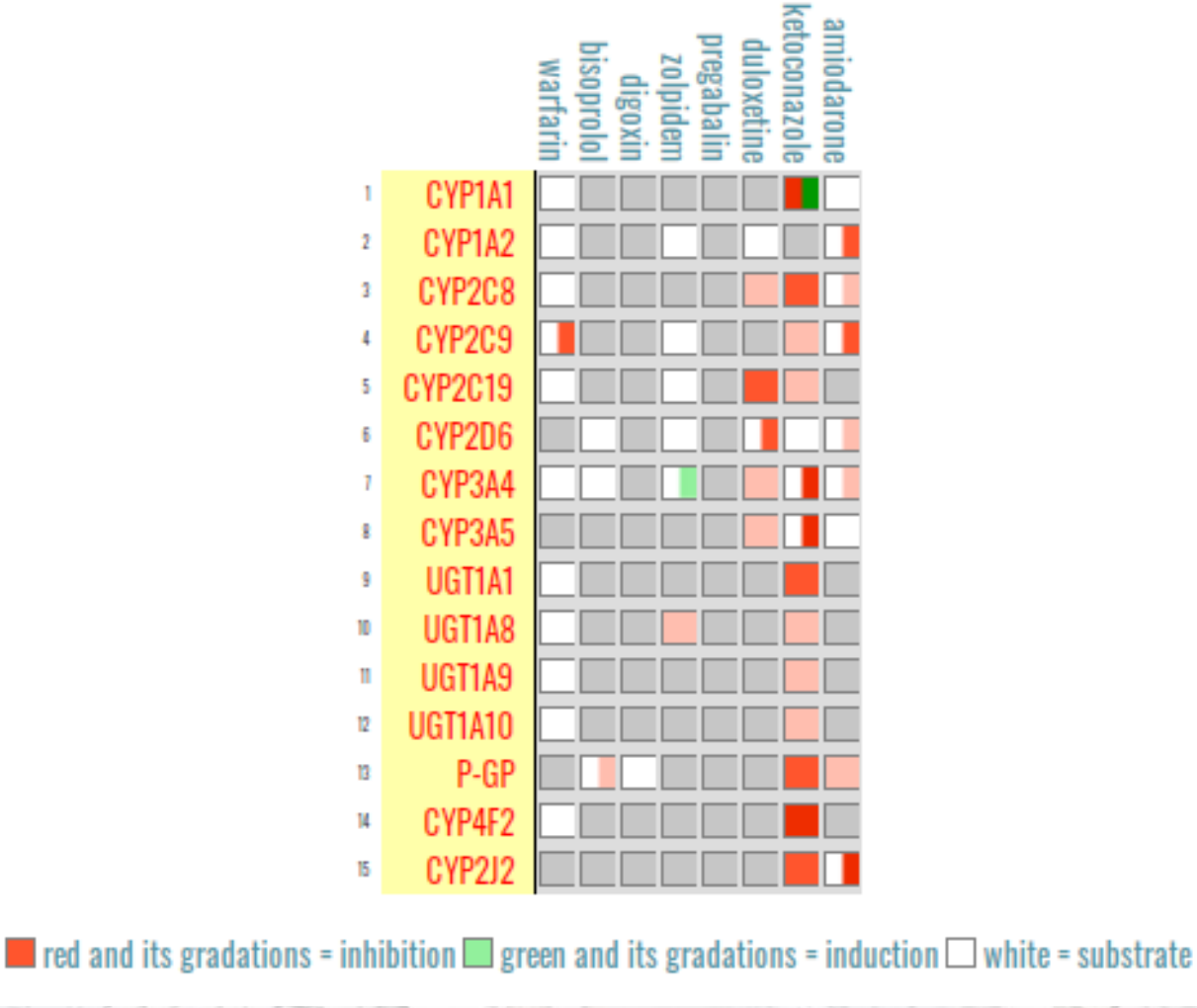
ASSESS THE SIDE EFFECTS

POSSIBLE SUMMATION OF ADVERSE REACTIONS / SIDE EFFECTS

	warfarin	bisoprolol	digoxin	zolpidem	pregabalin	duloxetine	ketoconazole	amiodarone
hyponatremia						■		■
hyperkalemia		■	■				■	
agranulocytosis								■
hypomagnesemia		■						
hyperglycemia					■	■		
aplastic anemia								■
hemolytic anemia								■
thrombocytopenia		■	■				■	■
leukopenia					■			■
eosinophilia			■					■
hypoglycemia		■			■		■	
CPK elevation					■	■		
urinary dyschromia	■							
neutropenia					■			■

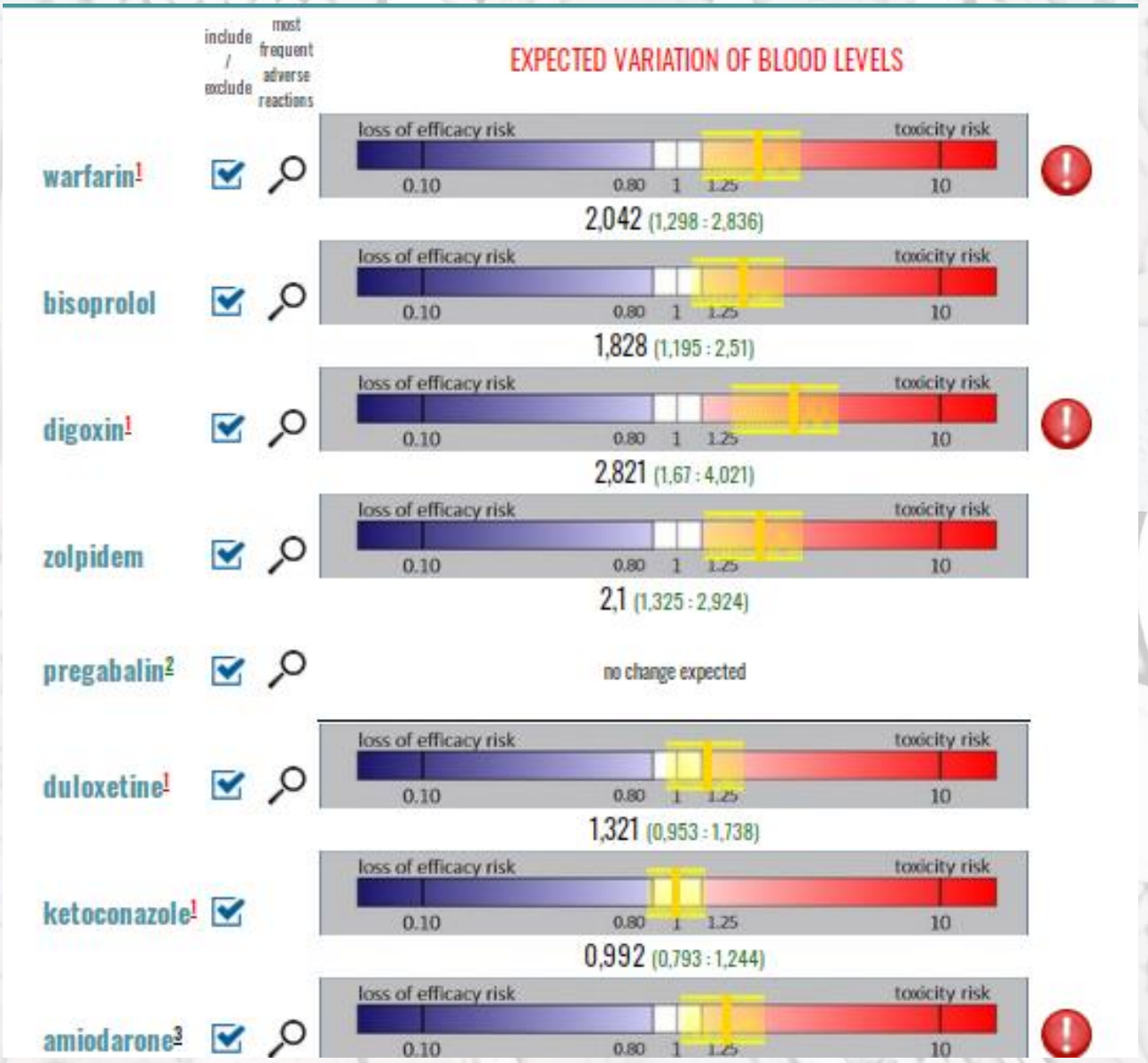
- ✓ You may have an overview of the possible undesired effects of the chosen combination, divided by apparate, to better understand what is happening to your patient
- ✓ For many situations you'll may find suggestions, from the scientific literature, on how to deal with any undesirable effects that require intervention

TOWARD A PHARMACOKINETIC HYPOTHESIS



- ✓ 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).

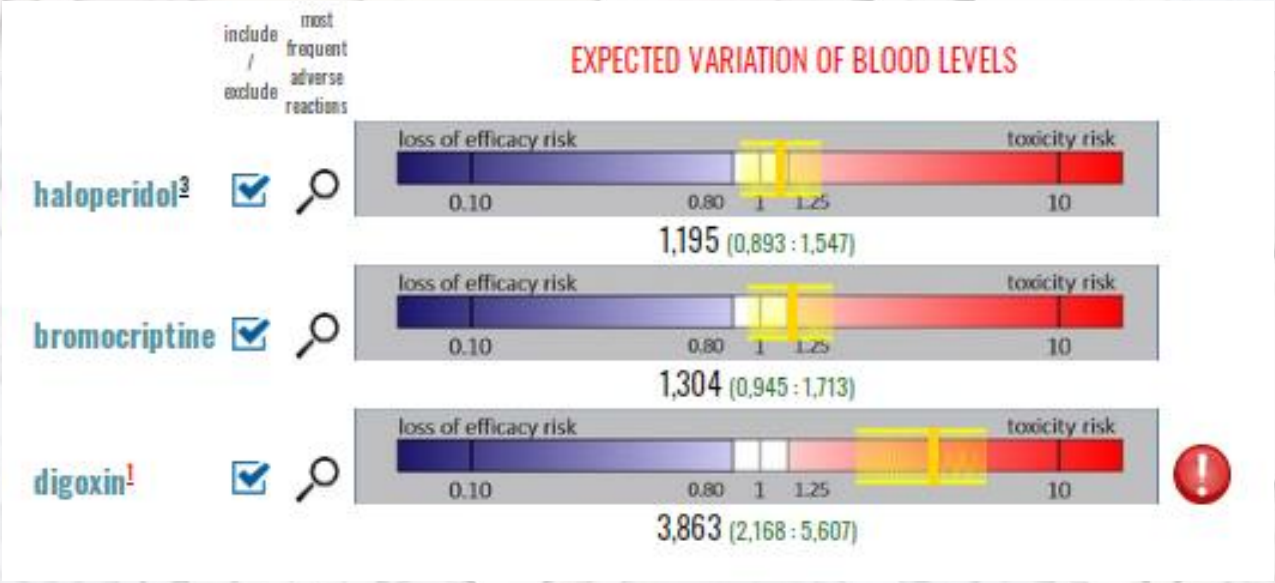
TOWARD A PHARMACOKINETIC HYPOTHESIS



- ✓ 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.

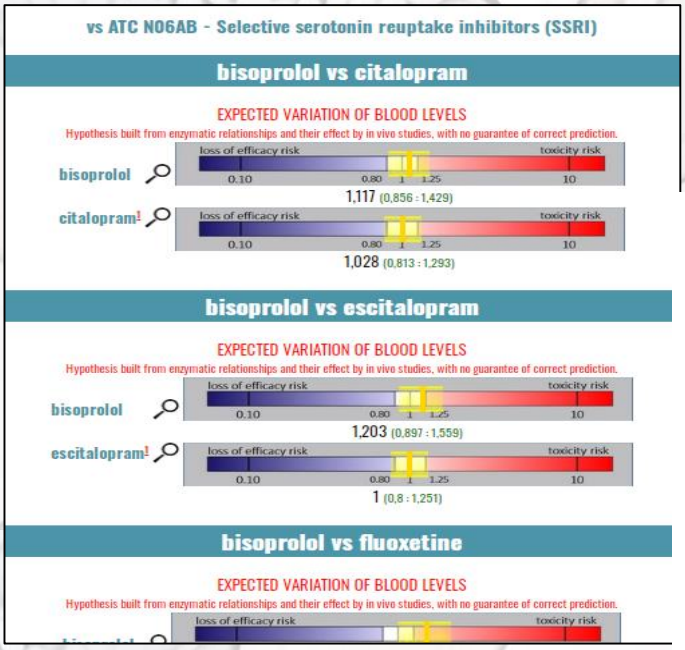
AVOID SERIOUS ERRORS

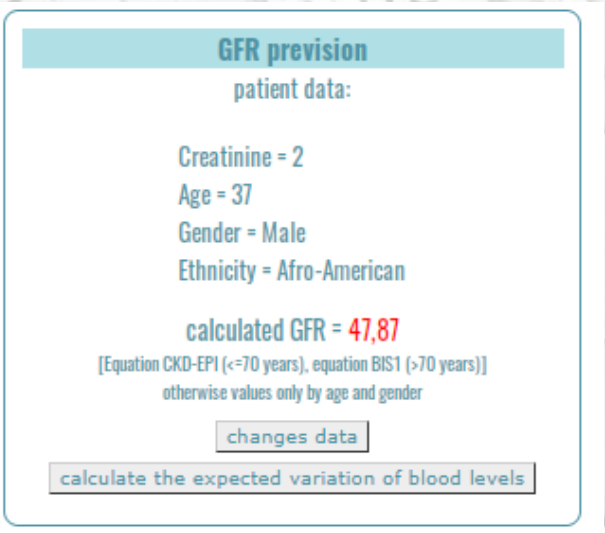
- ✓ AVOID TO ADMINISTER TO THE PATIENT CONTRAINDICATED THERAPIES WITHOUT EVEN BEING AWARE OF THIS.
  A lot of criticalities are cryptic and impossible to remember, for example: "CONTRAINDICATED with CYP3A4 substrates that prolong QTc" or "AVOID with strong CYP2C9 inhibitors" or "NOT RECOMMENDED with ototoxic drugs". There are over 150 categories of this kind in the package inserts.

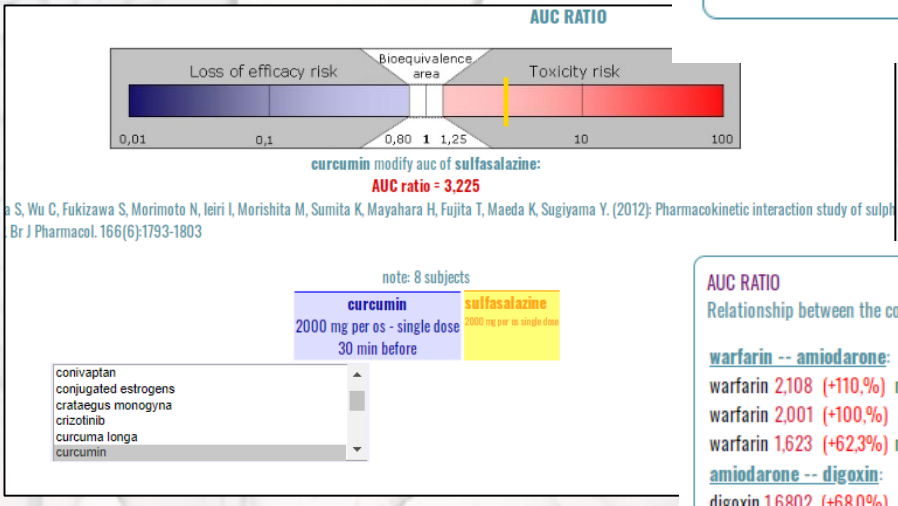


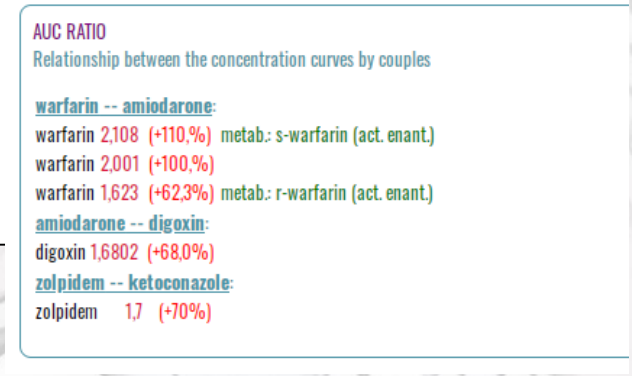
- ✓ IDENTIFY HIGHLY DANGEROUS SITUATIONS,
  also «quoad vitam»: only an overall view of pharmacokinetics, a peculiarity of this instrument, can allow it.
  Mere evaluation by pairs exposes to very serious errors, huge damages for the patient and heavy professional responsibilities.

AND OTHER TOOLS…









…FOR THOSE WHO WANT TO DISCOVER THEM

INTERACTIONS EXPLORER

duloxetine

General info:
CYP1A2 and CYP2D6 substrate. Coadministration of duloxetine with potent CYP1A2 inhibitors should be avoided. Caution is advised in using duloxetine with drugs that inhibit CYP1A2 metabolism or with potent CYP2D6 inhibitors. CYP1A2 and CYP2D6 inhibitor. Caution with drugs that are extensively metabolized by CYP2D6 and that have a narrow therapeutic index. Highly bound (> 90%) to proteins in human plasma: with another drug that is highly protein bound this may cause increased free concentrations of the other drug. Drugs that raise the gastrointestinal pH may lead to an earlier release of duloxetine. The risk of blood pressure decreases may be greater with concomitant medications that induce orthostatic hypotension. Caution about the risk of bleeding with drugs that affect coagulation. + -

Lab tests interactions:
no interaction or no data in the database

Interactions with food intake:
Food does not affect the Cmax of duloxetine, but delays the time to reach peak concentration from 6 to 10 hours and it marginally decreases the extent of absorption (AUC) by about 10%. Duloxetine should be swallowed whole and should not be chewed or crushed, nor should the capsule be opened and its contents be sprinkled on food or mixed with liquids. All of these might affect the enteric coating.

More common adverse events:
More common adverse reactions (>=5%): nausea, dry mouth, somnolence, fatigue, constipation, decreased appetite, and hyperhidrosis

Decrease in efficacy

LETTER TO THE DOCTOR

Dr.

- 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

add any text

- add the pharmacodynamic toxicities graph
- add the enzymatic relations graph
- add the the expected AUC change graph

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 46-year-old female was receiving a total weekly dose of 56 mg of warfarin. During the 4 months prior to the incident INR, her average INR was 2.0, with a range of 1.6-2.2, while taking the same weekly dose of warfarin. Her INR increased to 4.6 after drinking approximately 1.5 quarts (1420 mL) of cranberry juice cocktail daily for 2 days. Her INR 14 days later without cranberry juice cocktail consumption was 2.3. For the next 3 months, while taking warfarin 56 mg per week, her average INR was 2.1, with a range of 1.4-2.5. At a subsequent visit, after drinking approximately 2 quarts (1893 mL) of cranberry juice cocktail daily for 3-4 days, her INR had increased to 6.5. Her INR after holding warfarin for 3 days was 1.86. Her INR 7 days after resuming the weekly dose of warfarin 56 mg was 3.2. During both of the elevated INR episodes, no other factors were identified that would have resulted in an elevated INR, such as drug, herbal, disease, or other food interactions. An objective causality assessment revealed the interaction was highly probable.Warfarin is the most commonly used anticoagulant for chronic therapy. There have been several case reports of cranberry juice or cranberry sauce potentiating the effects of warfarin by elevating the INR; however, clinical trials evaluating this interaction have failed to demonstrate a significant effect on an INR. Our case report describes INR elevations in a patient previously stable on warfarin after ingestion of cranberry juice cocktail daily for several days. This elevation occurred on 2 separate occasions, which distinguishes our case from other published literature.

Ann Pharmacother. 2011 Mar;45(3):e17. doi: 10.1345/aph.1P451. Epub 2011 Mar 1. Warfarin-cranberry juice interaction. Hamann GL, Campbell JD, George CM.

PUBMED

This case reports on a patient whose International Normalized Ratio (INR) increased after ingestion of cranberry sauce 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 on chronic warfarin therapy for atrial fibrillation experienced INR elevations of two- to three-fold after two separate ingestions of cranberry sauce. In each case, her INR values decreased after withholding three to four doses and resuming a similar maintenance dose of warfarin. Although the majority of the pharmacokinetic and pharmacodynamic studies did not find a significant interaction between cranberry and warfarin, several case reports indicate that cranberry products may increase INR values in patients on warfarin. Practitioners should consider cranberry usage as a potential contributor in the evaluation of supratherapeutic INR values in patients on warfarin.

Consult Pharm. 2012 Jan;27(1):58-65. doi: 10.4140/TCP.n.2012.58. Cranberry and warfarin interaction: a case report and review of the literature. Haber SL, Cauthon KA, Raney EC.

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