Behind CYP450 interaction tables – the effect of gender and age on pharmacokinetics



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METHODS

A systematic **online literature** research was performed on usual platforms. 168 references could be evaluated.

BACKGROUND AND OBJECTIVES

If not incorporated as physiological substrates, drugs and food components are identified as **xenobiotics**. The risk of interactions increases with the number of substrates administrated. Interaction tables are restricted to unspecific isoenzymes of the families CYP1, CYP2, and CYP3. Data on gender impact has been required by the FDA only after 1993. The aim of this work was to assess the impact of gender and age on pharmacokinetics.

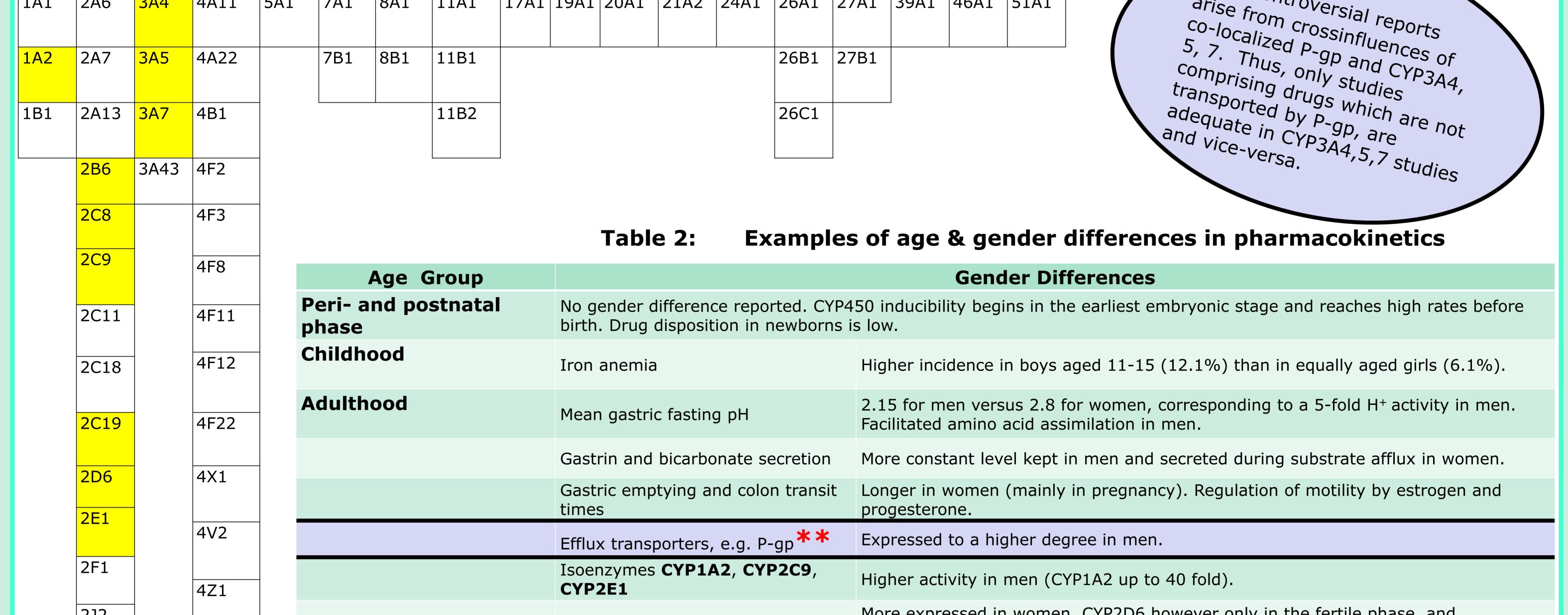
RESULTS

Cytochrome P450 isoenzyme subfamilies comprised in the most used drug interaction table (i.e. Flockhart, retrieved from http://medicine.iupui.edu/clinpharm/ddis) are 1A2, 2B6, 2C9, 2C19, 2D6, 2E1, and 3A4/5/7. Other isoenzyme subfamilies according to SuperCYP (http://bioinformatics.charite.de/supercyp), Drugbank (http://www.drugbank.ca), or Uniprot (http://www.uniprot.org) are not duly known in practical pharmacology, partly because of their predominant extrahepatic tissue specificity. However, their importance for local adverse reactions may be considerable. Of a total of 57 human isoenzymes CYP450, only 10 subfamilies are currently used by physicians and pharmacists as interaction references in the practice (Table 1).

Table 1: Human CYP450 isoenzymes

17A1 | 19A1 | 20A1 | 21A2 | 24A1 26A1 27A1 39A1 46A1 2A6 8A1 1A1 3A4 4A11 7A1 11A1 51A1 5A1

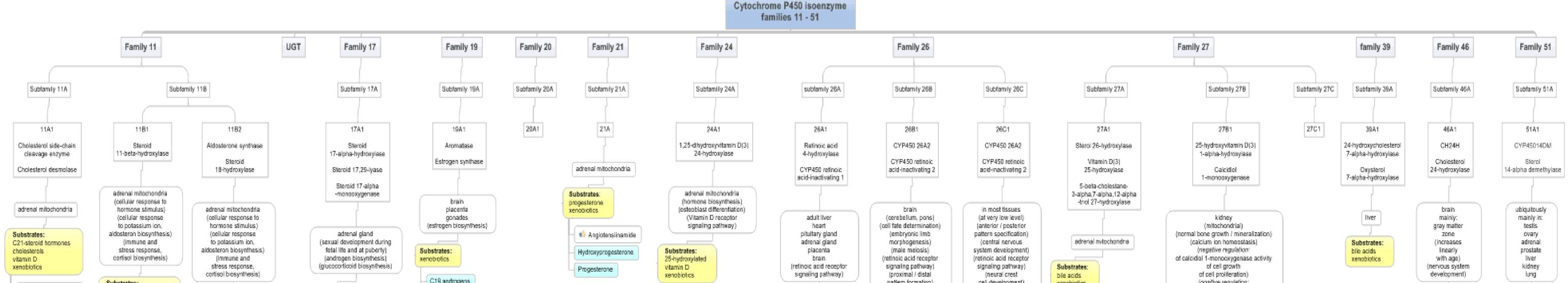




2J2 2R1	Isoenzymes CYP3A4,5,7, CYP2A6, CYP2B6, CYP2D6	More expressed in women. CYP2D6 however only in the fertile phase, and CYP3A4,5,7 depending on the menstrual cycle with top levels before ovulation and in pregnancy.
2S1	Plasma levels of copper and ceruloplasmin	Contraceptives in women aged 20-39 increase plasma levels of copper and ceruloplasmin, but not its absorption.
	Copper absorption	Higher in women aged 20-59 (71%) than in men of the same age (64%). This difference does not exist in both genders aged 60-83.
2U1 2W1	Protein digestion resistance	Protein digestion resistance due to PPI treatment in pregnancy is a documented risk factor of predisposition to immune responses and asthma of the child (5.6% versus 3.7% in the population). In pregnancy, trophokinetics change as a result of high progesterone levels, altered hemodynamics, cardiac output, etc.

Figure 1: CYP450 Isoenzymes Families 11-51

Cytochrome P450 isoenzyme families 11-51 as an extract of all 57 CYP450s featuring synonyms, tissue specificity, eventually biological function, and substrates. Green background: substrate is naturally occurring, no symbol: substrate, con icon: inhibitor, pro icon: inducer.



Adilocidica		cortisol biosynthesis)	(grades deal deal in tan)	· · · ·	Progesterone	xenobiotics	signaling pathway)	(proximal / distal	(neural crest	ble adds	of cell proliferation)	development)	lung
	Substrates:			C19 androgens				pattern formation)	cell development)	xenobiolics	(positive regulation:		
- 🌻 Aminogiuthetimide	11-beta steroids		Substrates:					(spermatogenesis)	(organelle fusion)		of keratinocyte differentiation		
	(18- or 19-hydroxylation)	Substrates:	xenobiolics	— 🥺 Aminoglutethimide		25-hydroxyvitamin D3	Substrates:			Alterestelated	of vitamin D 24-hydroxylase activity	Substrates:	Substrates:
 Androstanolone 	androstendione	xenobiotics				(Calcidiol)	retinoic acids			- Alfacalcidol	of vitamin D receptor signaling	cholesterol	xenobiotics
	(aromatization)			- 🥺 Anastrozole		1-alpha,25-dihydroxyvitamin	xenobiotics	Substrates:	Substrates:	E hata shalastana	pathway)	xenobiofics	
 Angiotensinamide 	xenobiotics	Aldosterone	Aldosterane			D3 (Caldtriol)		retinoic acids	retinoic acids xenobiotics	5-beta-cholestane -3-alpha,7-alpha,12-alpha-triol	(response: to estrogen stimulus		Lanosterol
				Androstanolone			- Acitretin	xenobiotics	xenodicites	combinets only on the other	to interferon-gamma	Choiesterol	
- 🥶 Clomifen	 Aldosterone 	- 🍳 Aminogluthetimide	- 🤗 Aminogluthetimide			Cholecaloferol				25-hydroxyvitamin D3	to lipopolysaccharide		- 👎 Fluconazol
		· · · · · · · · · · · · · · · · · · ·	(technologies)	- 📫 Betamethason			 all-trans retinoic acid 	all-trans retinoic acid	 all-trans retinoic acid 	(Calcidiol)	to tumor necrosis factor	 Dextrometorphan 	- 11000110201
- Cholesterol	— 🌻 Aminogluthetimide	- 📣 Aminosalicy is acid	Aminophenazone			- Ergocalciferol		(preferred)			to vitamin D)		Itraconazol
		an Antrosalcyte and	Androstancione	- 🥺 Bifonazole			9-dis-refindic add	O are estimate a stat	9-cis-retinoic acid	- Cholecal ciferol		 Diciofenac 	
- 📣 Corticotropin	 Androstendione 	Acaleteoriesmide				 Paricalcitol 	Continute	9-dis-refinoic add	(preferred)		Substrates:	Biomenetic	- Cetoconazoi
		Angiotensinamide	- 🤨 Dexamethason	- 📫 Bucladesine			Eletrinate	13-cis-retinoic acid		- 🤨 Giolosporin	25-hydroxylated	Phenacetin	
 Desoxycortone 	 Angiotensinamide 	(1 Provent	+ Dexametrazion			Teriparatide					vitamin D	Progesterone	(The second
		🤍 Benazepri	👘 Matasiasimaida	🚽 📫 Buserein			Ketoconazole	Eletrinate		 — Oprofibrate 	xenobiotics		- 🤨 Meglutol
— 🏴 Dexamethason	- 🡎 Cimetidine	Desoxycortone	- Metocloprmaide				(d a u a)					Testosterone	
				Clofenotane			- Carlinol			- 🖒 Colestyramin	25-hydroxyvitamin D3 (Calcidiol)		- 🡎 Miconazol
 Dinoprostone 	— 🌻 Ciotrimazola	🤨 Eplerenone	- 🤗 Pregnenoione	Cideliolalle							20-hjaloký hamil 20 (daolatel)		(1
		Epierenblie	Progesterone	Ciomifene						— 📫 Dexamethason	1-alpha,25-dihydroxyvitamin		- 🤗 Sertaconazole
- 🥶 Gluthetimide	- 📫 Corticotropin	🤨 Etomidate	r logostelone	Ciomirene							D3 (Calcitriol)		
		Exonicane		Confusional Retensions									Terconazol
- 🤨 Ketoconazole	 Desoxycontone 			Conjugated Estrogens							Ergocalciferol		
		- 🧐 Glucose		Danazol									
 Omeprazole 	— 😐 Dexamethason	Hydrocortisone											/
		The second second		Diethyistibestrol									/
 Sequinavir 	— 🌻 Etomidate												/
				Exemestane									/
Terbinaline	— 🌻 Fluconazola												/
				Letrozole									/
	 Hydrocortisone 			Tuttututu									/
				Testolactone									
	 Metoconazole 			Testosterone									
	11-beta Steroids												

CONCLUSIONS: Gender and life-phase differences (Table 2) exert an important impact on digestion of food components. Research on nutrients in this domain, hardly existing so far, remains to be established.

Conflicts of interest: The authors have declared no conflicts of interest.