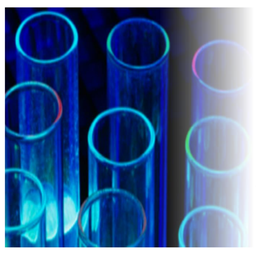

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CONSEQUENCES OF THE DIFFERENT ENZYME ALLELES REGARDING ALCOHOL TOLERANCE AMONG POPULATIONS.

Lorena Olmo Pérez

OBJECTIVES

THE PURPOSES OF THIS STUDY ARE THE FOLLOWING:

1. **TO GIVE A DEEPLY EXPLANATION OF THE PROCEDURE OF THE ETHANOL'S METABOLISM.**
2. **TO KNOW THE POLYMORPHISM THAT THESE ENZYMES REPRESENT AND THE FLUCTUATION DURING THE PROCESS.**
3. **TO UNDERSTAND THE DIFFERENCES BETWEEN SUSCEPTIBILITY, RESISTANCE AND THE ADDICTIVE BEHAVIORS THAT APPEAR AMONG THE POPULATION RACES VERSUS THE ALCOHOL CONSUME.**
4. **TO SHOW THE EFFECT OF THE INTERACTION OF THE POLYMORPHIC ENZYME GENES.**

PROPERTIES ALCOHOL DEHYDROGENASE

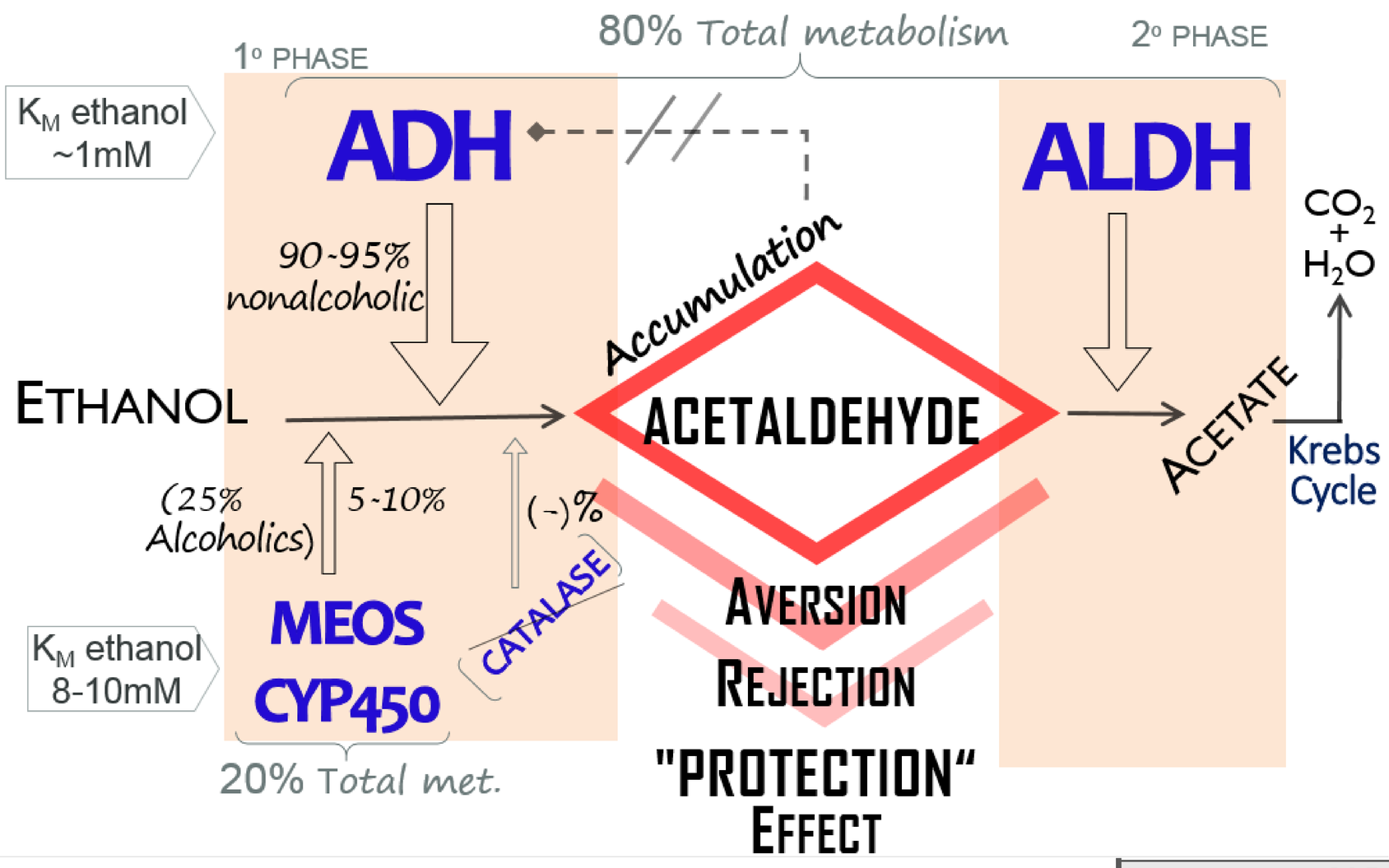
	α α	β1 β1	β2β2	β3β3	γ1γ1	γ2 γ2	π π
K_m ethanol (mM)	4,2	0,049	**0,94**	24	1	0,63	34
V_{max} (min^{-1})	27	9,2	**400**	**300**	87	35	20
pH optimum	10,5	10,5	**8,5**	**7,0**	10,5	10,5	10,5

(Crabb et al., 1987; Bosron et al., 1993)

ADH2 FREQUENCY

	% $ADH_2^1(\beta_1)$	% $ADH_2^2(\beta_2)$	% $ADH_2^3(\beta_3)$
White Americans	>95	<5	< 5
African-Black	85	<5	15
European white	85	15	< 5
Japanese Asian	15	85	< 5

(Bosron et al. (1993) & Crabb (1995).



C2 CYP450 ALLELE FREQUENCY

Population	CYP450 c2 allele frequency (%)
Asian	24
Afro-American	0,3 -1
White Brazilians	7
No White Brazilians	3

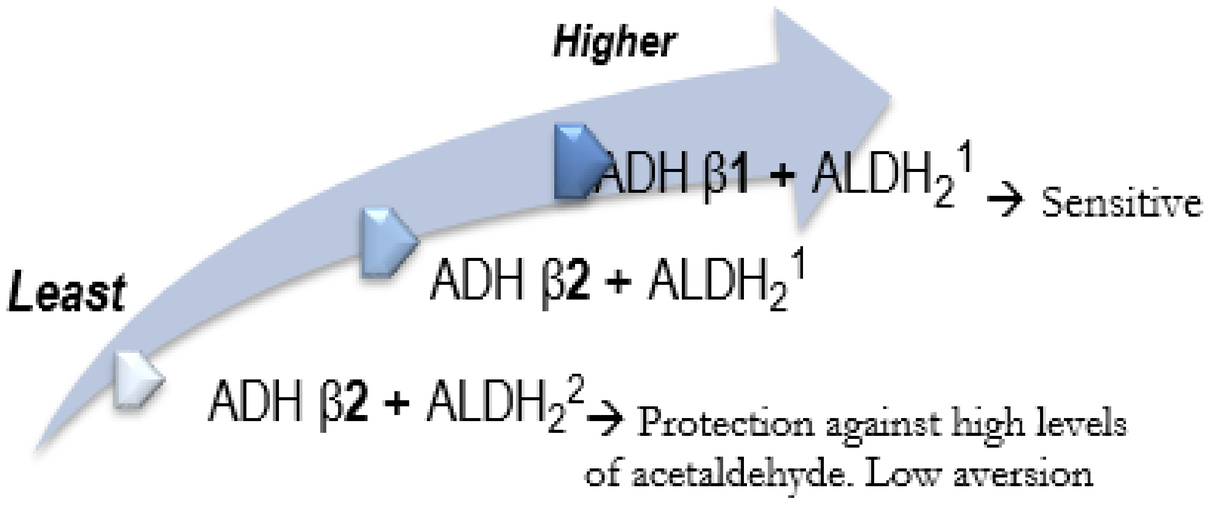
(Stephens (1994), Wang et al. (1999), Rossini et al. (2006).

$ALDH_2^2$ FREQUENCY

POPULATION	$ALDH2^2$ FREQUENCY
Asian	40 %
Other	Low or nonexistent
Alcoholic	2%
Nonalcoholic	40 %

(Stoil (1988), Xiao (1995), Lieber (1997), Yokoyama (1999)

RISK OF ALCOHOLISM IN INDIVIDUALS CARRYING.



PROPERTIES ALDH ISOENZYMES

ISOENZYME	ACETALDEHYDE KM	NAD⁺KM	
ALDH1	30 µM	8 µM	- Low contribution.
ALDH2 **$ALDH_2^1$ (ACTIVE)**	3µM	70 µM	- Principal responsible
$ALDH_2^2$ (INACTIVE) *E487K mutation.*	↓	↑	**- Lower activity for acetaldehyde**
ALDH3, ALDH4	↑↑		- Not important

(Sanchis et al. (1999), Perozich et al., (1999), Escarabajal (2003).

CONCLUSIONS

1. Alcohol degradation consists in two steps. Alcohol toxicity is due to acetaldehyde, an intermediate product.
2. The responsible enzymes of the metabolism are: ADH (main enzyme in the first step), MEOS, Catalase and aldehyde dehydrogenase (ALDH) (main enzyme in the second step). All of them present polymorphism with different kinetic properties that metabolize the toxic.
3. The ADH β2 and C2 allele of CYP450 have higher oxidative capacity, that produce more acetaldehyde accumulation. Due to its low oxidation activity, $ALDH_2^2$ inactive has the same effect. Accumulation of acetaldehyde causes people are less tolerant, causing a protective effect to alcoholism.
4. High oxidative capacity Allele and ALDH combination implies faster ethanol removal and better toxicity tolerance versus the ALDH inactive carrier. That's why humans with this combination consume more alcohol quantity and have bigger alcoholism risk.
5. This enzymes are common in Asiatic population. ALDH inactive is very low or nonexistent in Other populations. That explains the low tolerance to alcohol of the Asian population.