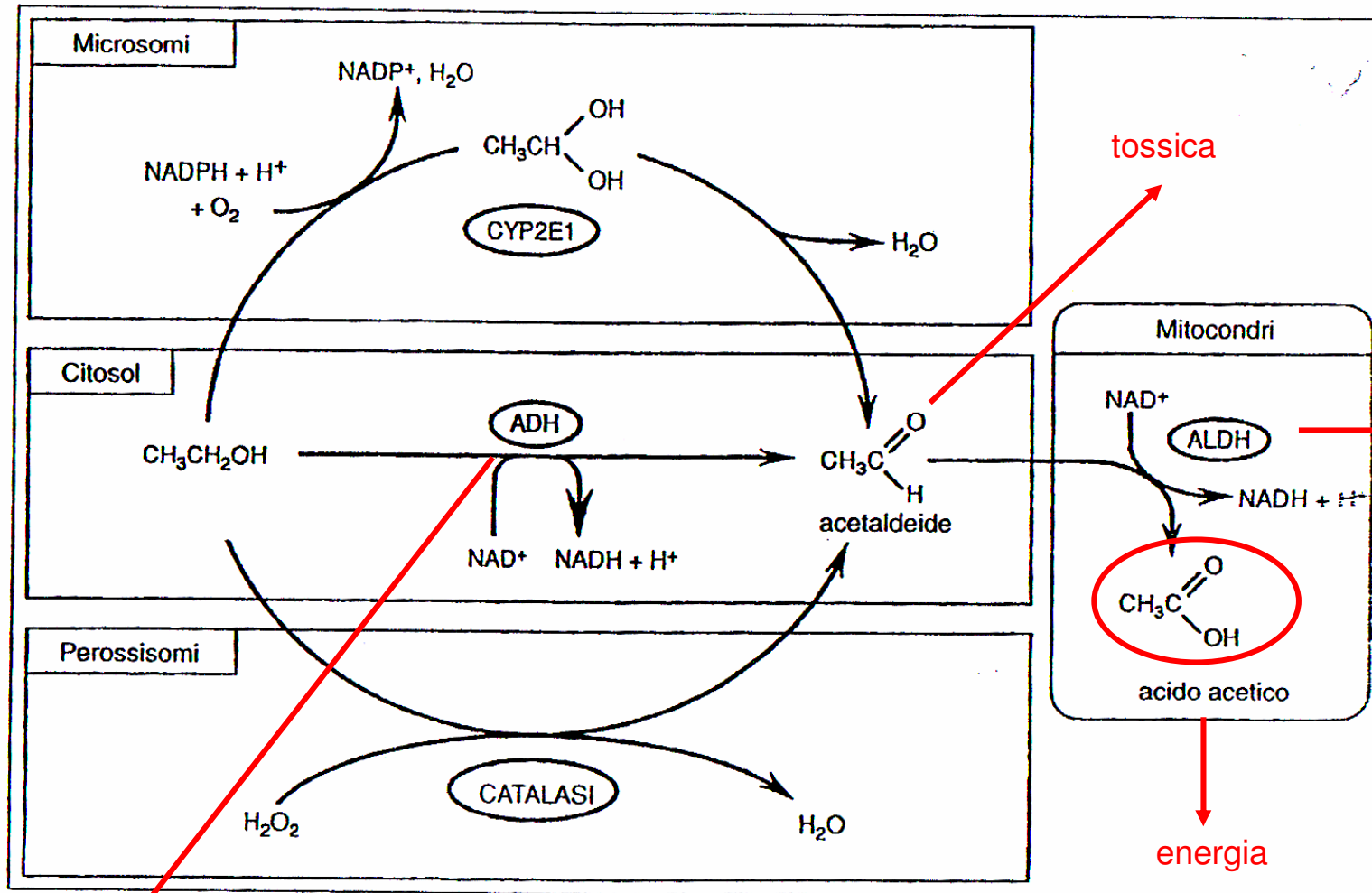


Enzimi del metabolismo degli xenobiotici

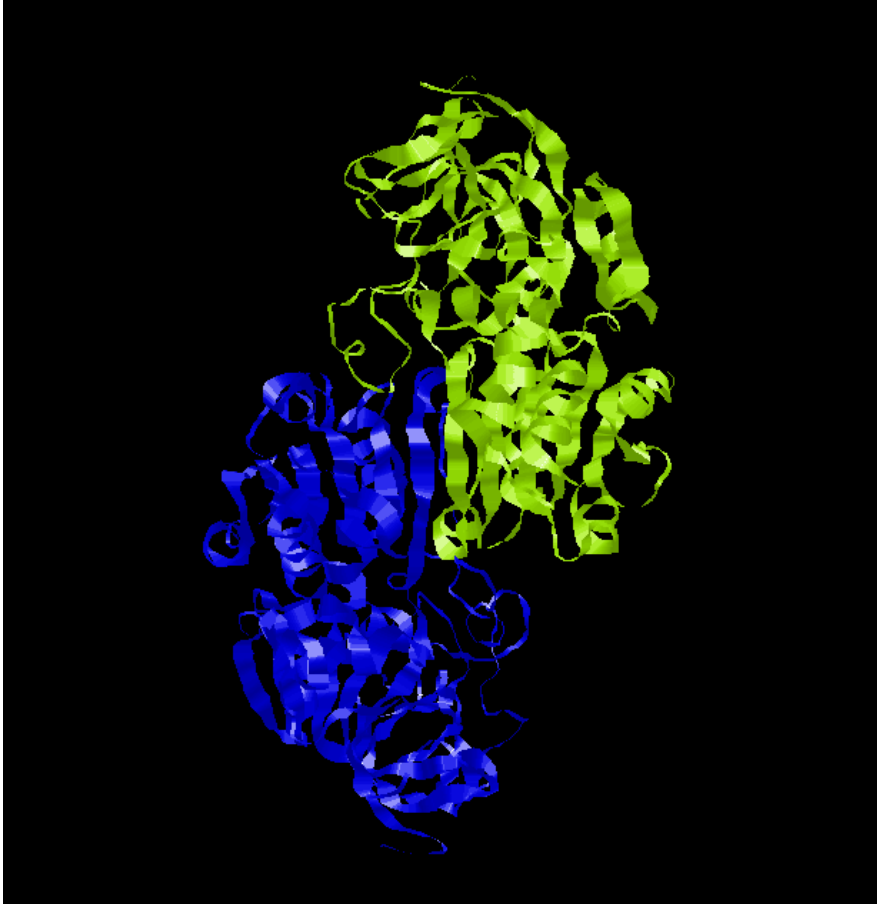
Tipi di reazioni	Enzima
Fase I Ossidazione	Citocromo P450 Alcol deidrogenasi Aldeide deidrogenasi Monossigenasi flaviniche Monoaminossidasi
Riduzione	Chinone reductasi (DT diaforasi) Citocromo P450 reductasi
Idrolisi	Epossido idrolasi
Fase II Coniugazione	UDP glucuronil transferasi Solfotransferasi N-acetil transferasi Metiltransferasi Coniugazione con amminoacidi Glutathione transferasi

Metabolismo dell'etanolo



Alcol deidrogenasi

Aldeide deidrogenasi



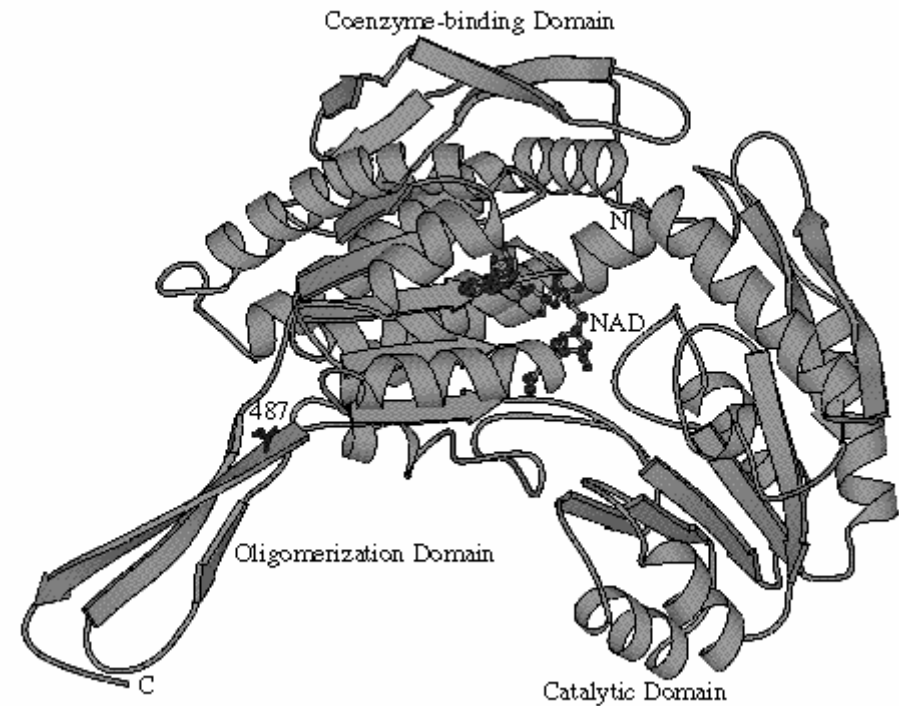
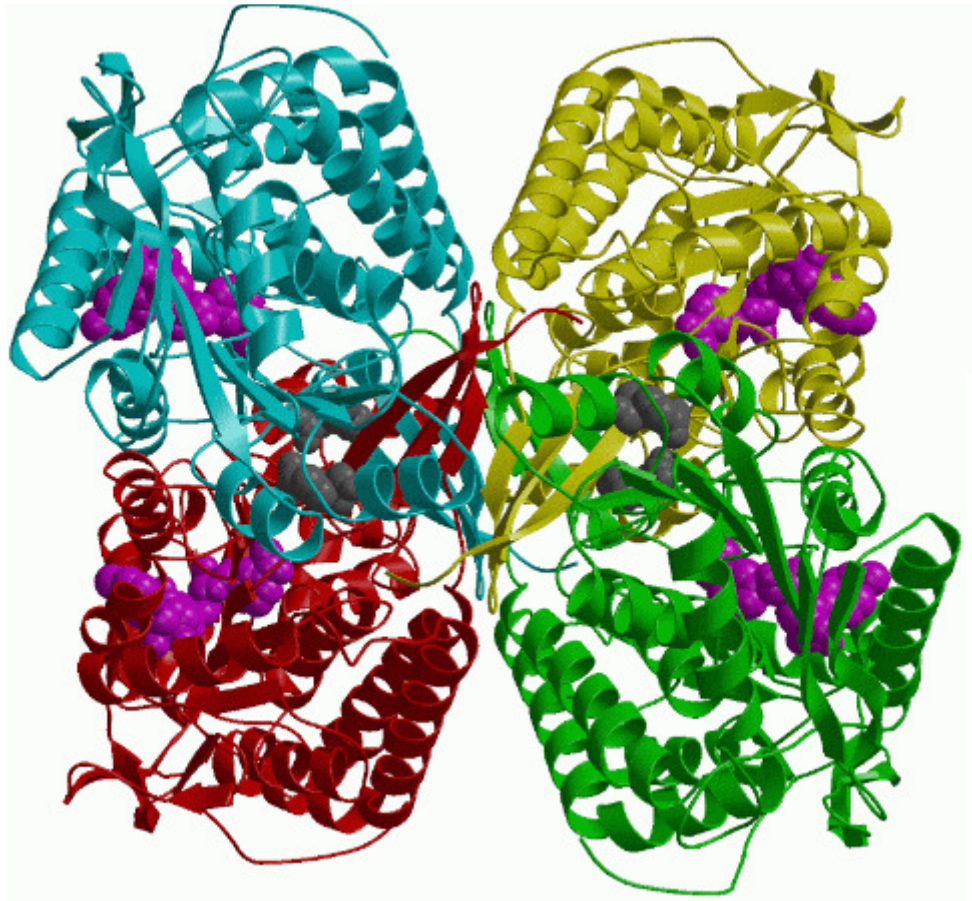
Alcol deidrogenasi:

enzima dimerico, citosolico

5 geni (α , β , γ , π , κ). B ha 3 alleli, γ 2 alleli

**Quindi 8 subunità diverse che si combinano
a formare isoenzimi con diversa efficienza
catalitica**

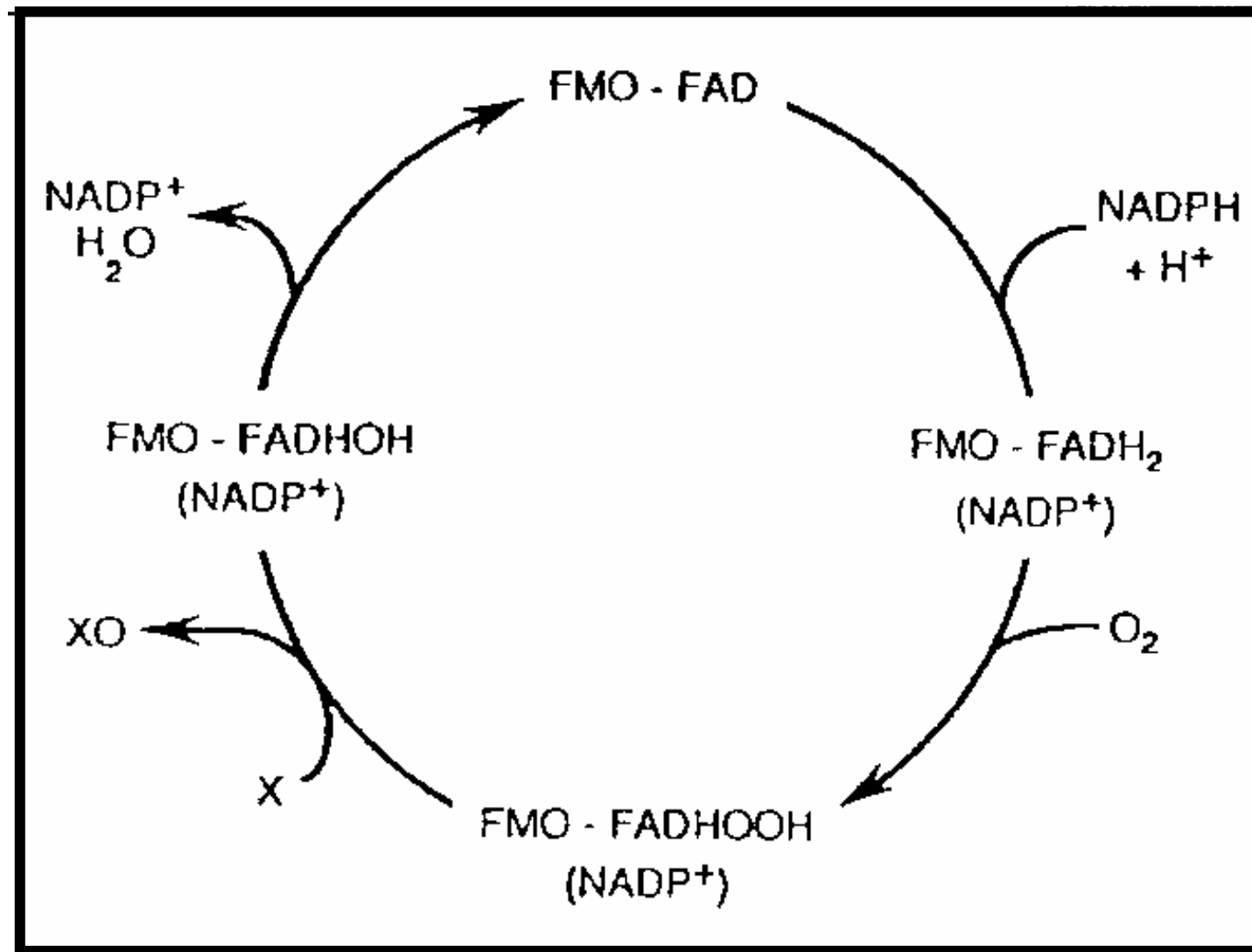
Gli isoenzimi presenti nelle popolazioni
asiatiche sono molto efficienti.



Aldeide deidrogenasi:

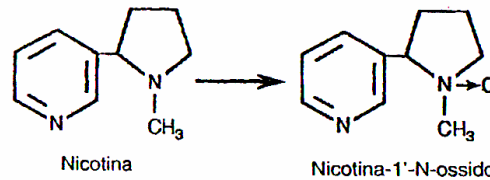
Nelle popolazioni orientali esiste un isoenzima con bassissima attività:
Intolleranza all'alcol("flushing syndrome").

FMO: MONOSSIGENASI FLAVINICHE DEL RETICOLO ENDOPLASMATICO

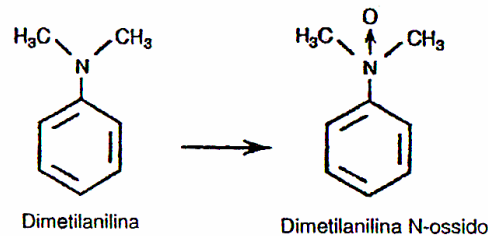


FMO: Ossidazione a livello di eteroatomi nucleofili: S, P, N

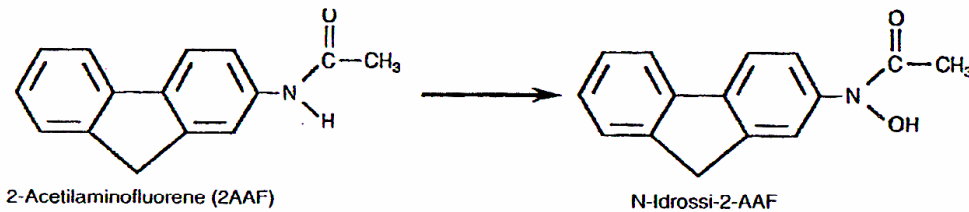
Amine terziarie (es. Nicotina, Clorpromazina, Flufenazina, Cocaina, Trimetilamina, Dimetilanelina, Desipramina)



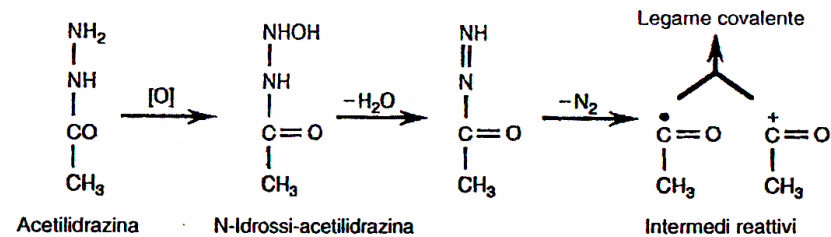
Amine secondarie (es. Dimetilanelina, Desipramina)



N-Acilarilamine (es. 2-Acetilaminofluorene)



Ildrazine (es. Acetilildrazina, Dimetilildrazina, Procarbazina, Benzilildrazina)

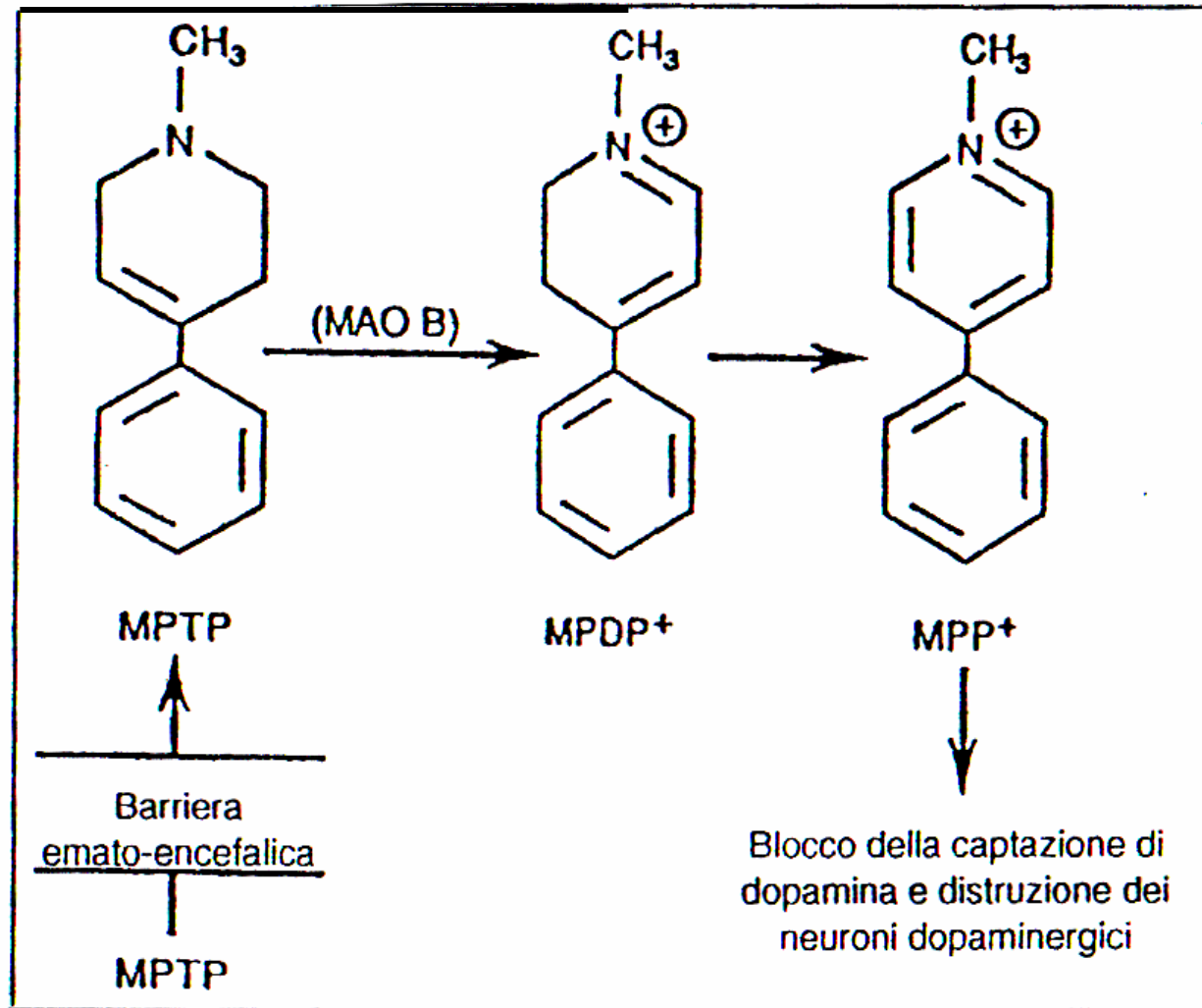


Monoaminossidasi (MAO)
flavoproteina mitocondriale.
Trasformazione di una ammina in una aldeide



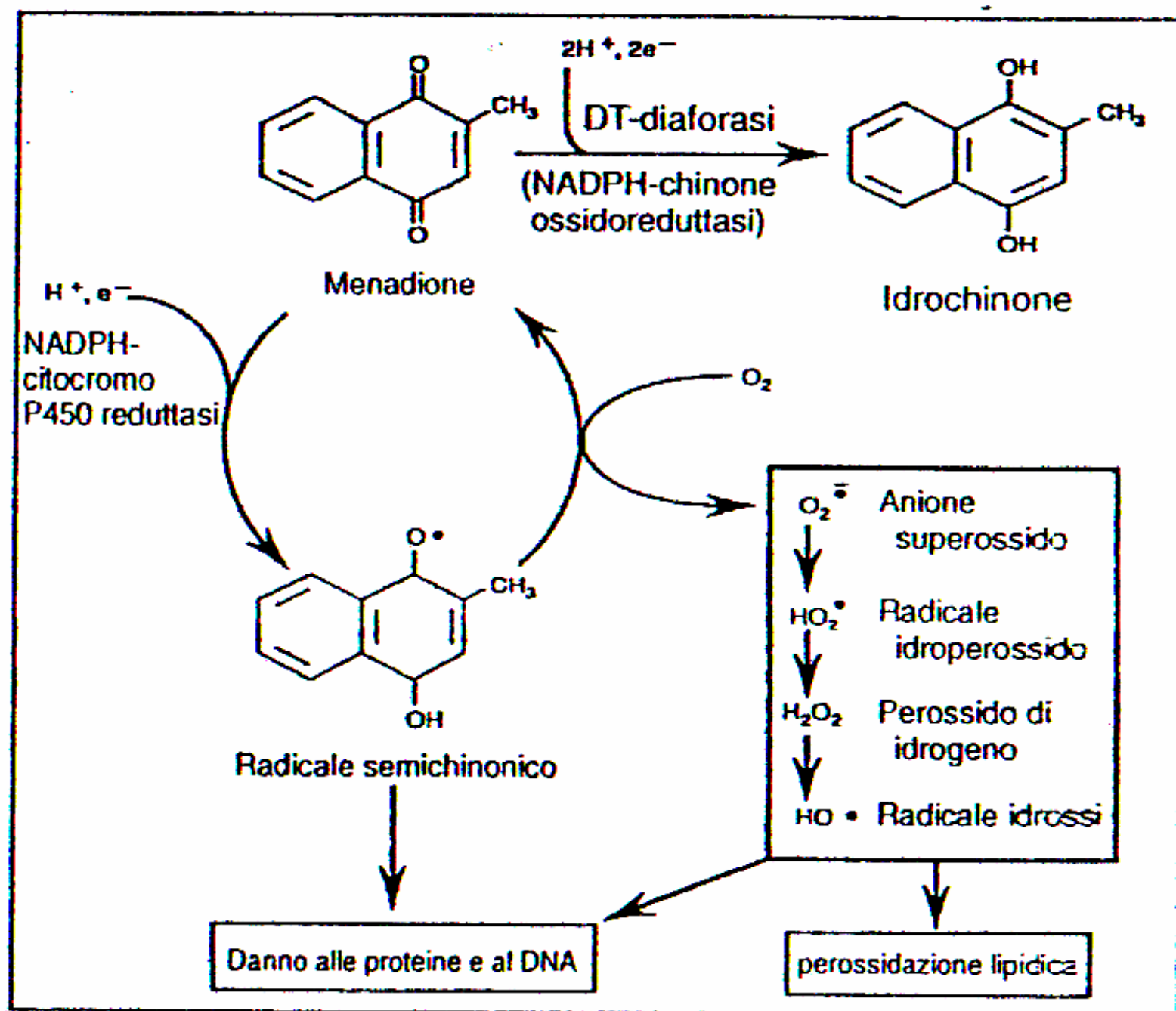
L'atomo di ossigeno incorporato nel substrato proviene dall' H_2O , ed i 2 elettroni sottratti al substrato vengono ceduti all' O_2 formando H_2O_2

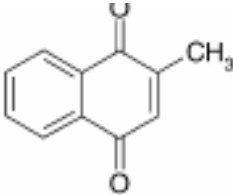
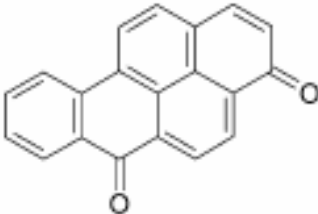
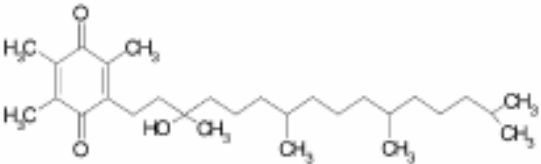
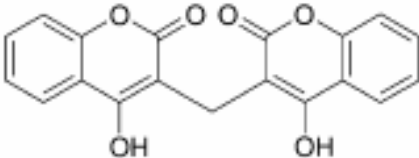
**Reazione catalizzata dalla monoaminossidasi (MAO):
1-metil-4-fenil-1,2,5,6-tetraidropiridina (MPTP)**



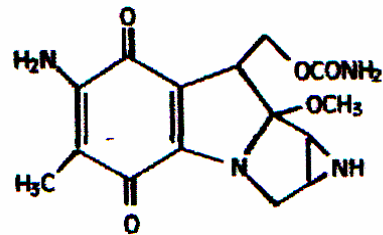
DT-diaforasi o NAD(P)H:chinone ossidoreduttasi 1 (NQO1)

- Enzima citosolico
- Omodimero (27 kDa per subunità)
- Flavoproteina (FAD)
- Catalizza la riduzione bieletronica di substrati di natura chinonica, in un singolo passaggio

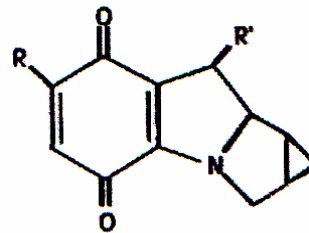


Menadione	Prototypical toxic redox-cycling agent and NQO1 substrate	
Benzo[<i>a</i>]pyrene-3,6-quinone	Toxic and mutagenic metabolite of benzo[<i>a</i>]pyrene. Generated by the cytochrome P450 system and detoxified by NQO1	
α -Tocopherol-quinone	Metabolite of α -tocopherol and potent lipid-soluble antioxidant. Maintained in reduced and active form by NQO1	
Dicoumarol	Inhibitor of NQO1 catalytic activity	

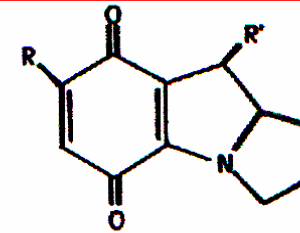
Farmaci antitumorali che vengono attivati dalla NQO1



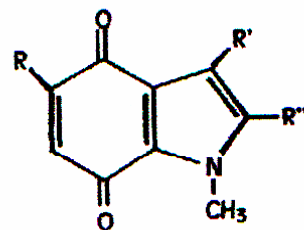
Mitomycin C



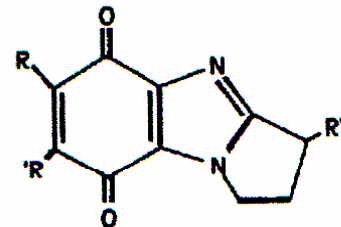
Cyclopropamitosene



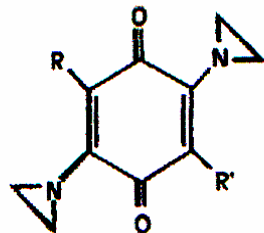
Mitosene



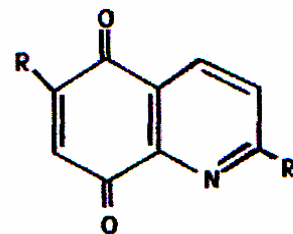
Indolequinone



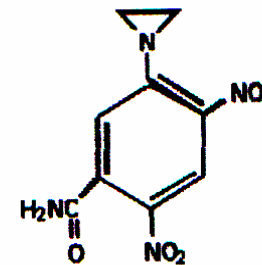
Pyrrolobenzimidazolequinone



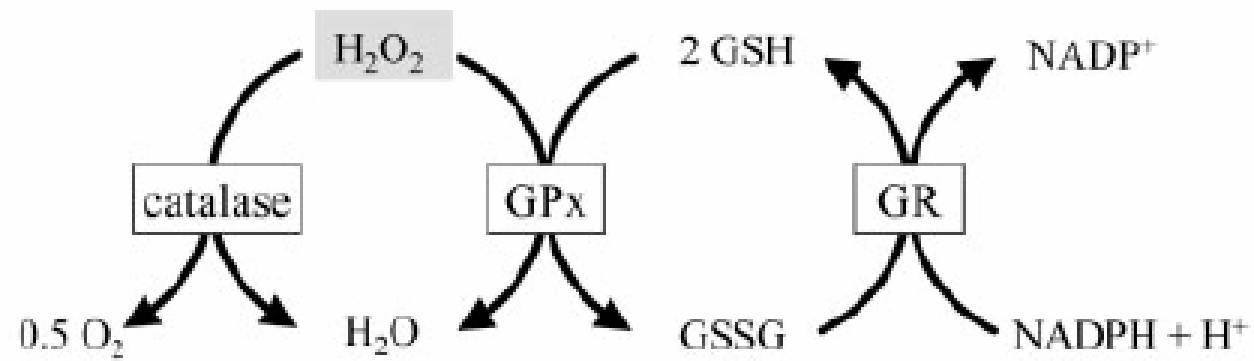
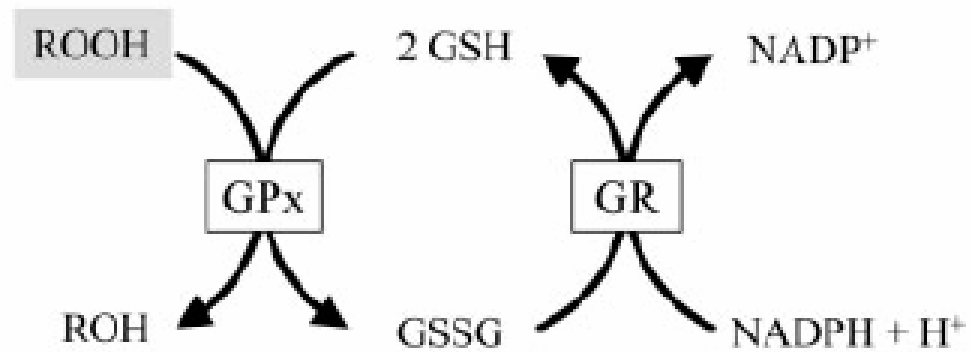
Aziridinybenzoquinone

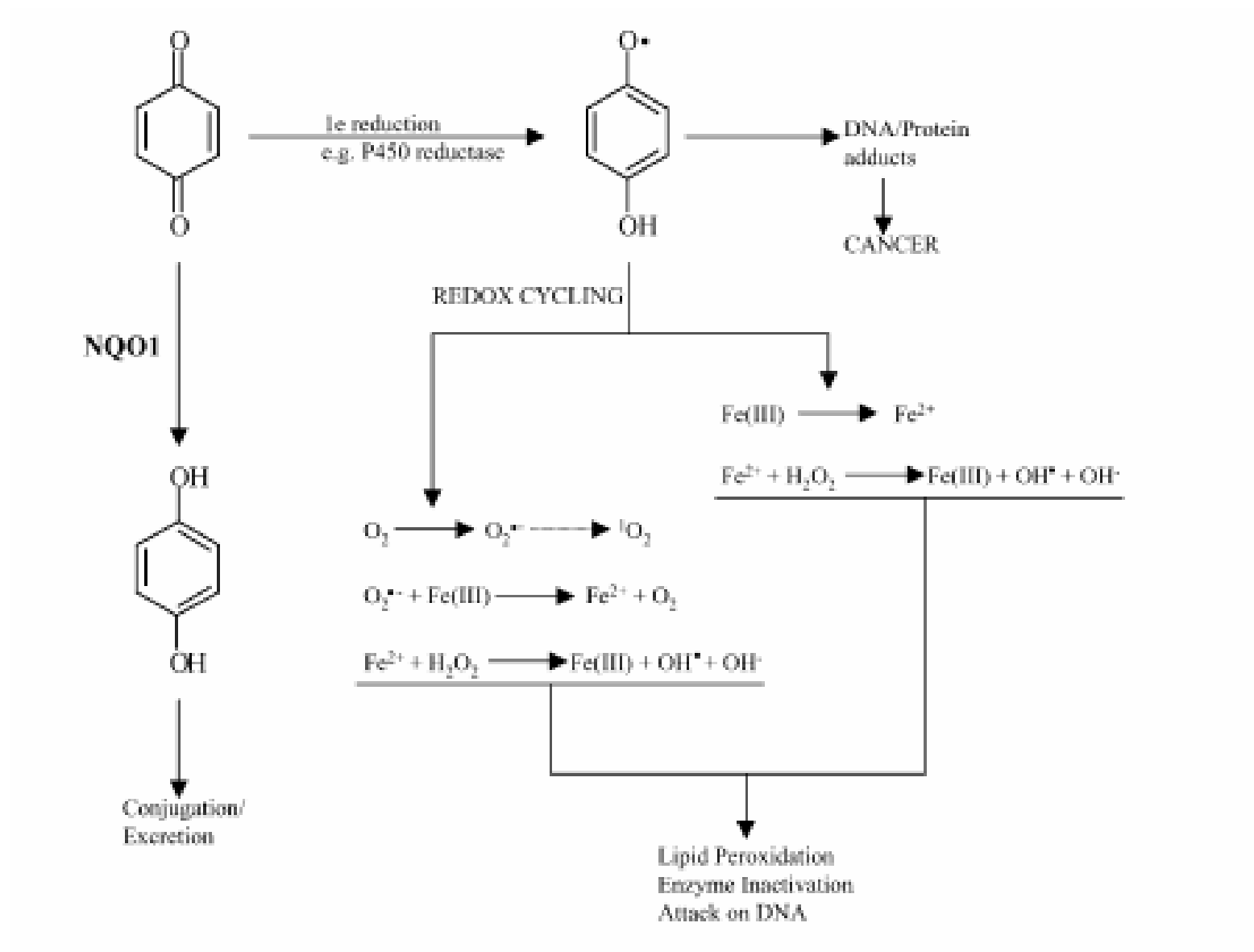


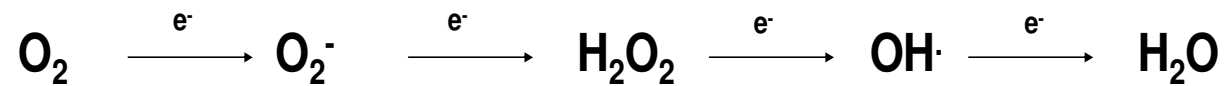
Quinolinequinone



CB1954

A**B**

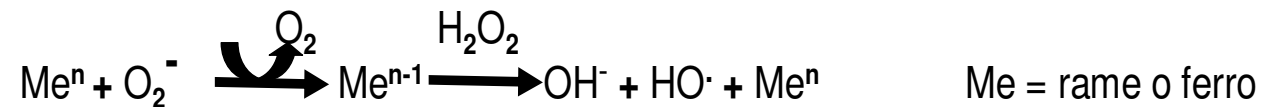




Autossidazione dell'ossiemoglobina
 NADPH ossidasi dei leucociti
 Catena di trasporto degli elettroni
 • mitocondri (nei siti dell'ubichinone e della NADH-deridrogenasi)
 • microsomi (citocromo P450 e citocromo P450 riduttasi)
 Enzimi citosolici: es. xantina ossidasi, aldeide ossidasi

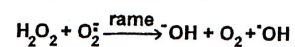
Dismutazione dell' $\text{O}_2^{\cdot -}$ spontanea o enzimatica (superossido dismutasi)
 Ossidasi perossisomiali: es. aminoacido ossidasi, urato ossidasi
 Amino ossidasi (diamino ossidasi, lisil ossidasi, monoamino ossidasi)

Reazioni tipo Fenton catalizzate da metalli:



Ossidasi
 Citocromo c ossidasi; ceruloplasmina plasmatica

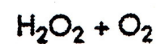
**Radicali liberi
dell'ossigeno**



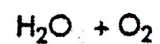
**Protezione
enzimatica**



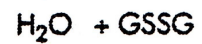
Superossido
dismutasi



Catalasi



GSH +
Glutathione
perossidasi



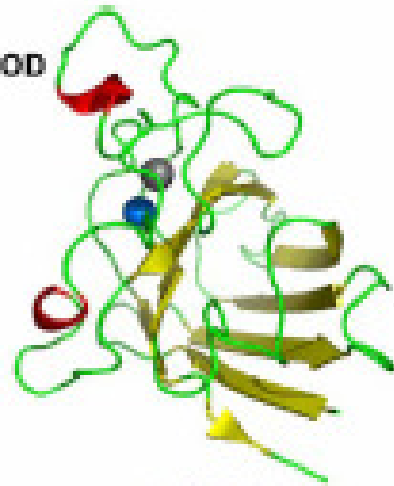
**Protezione
non enzimatica**

Alfa-tocoferolo
Beta-carotene
Ubichinone
GSH

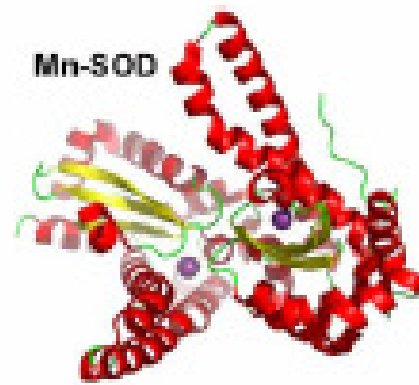
Distruzione

Lipidi
Proteine
Acidi Nucleici

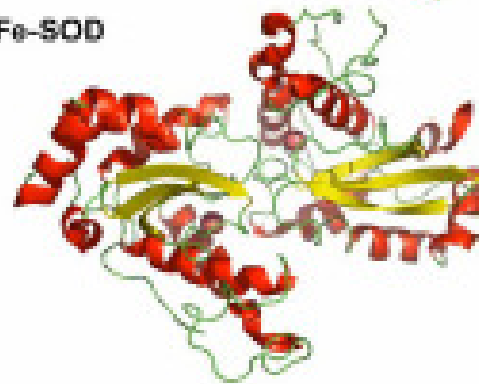
Cu,Zn-SOD



Mn-SOD

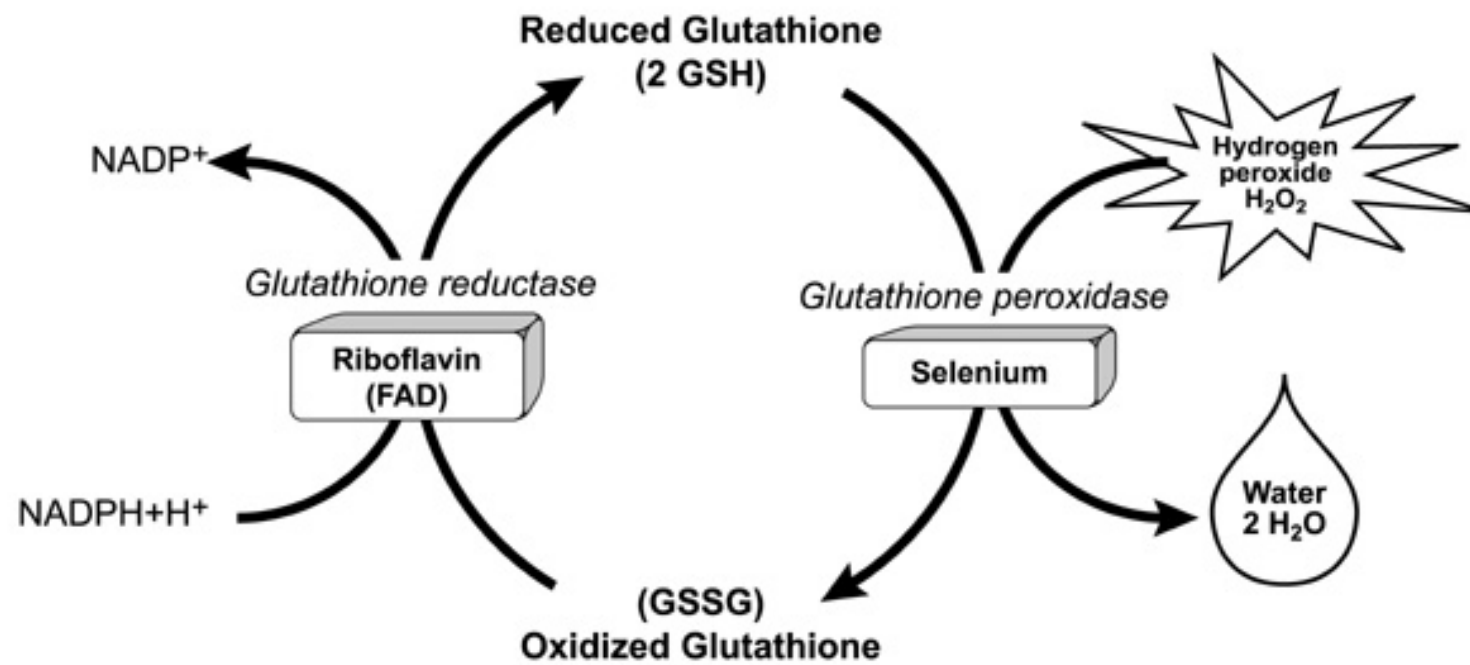


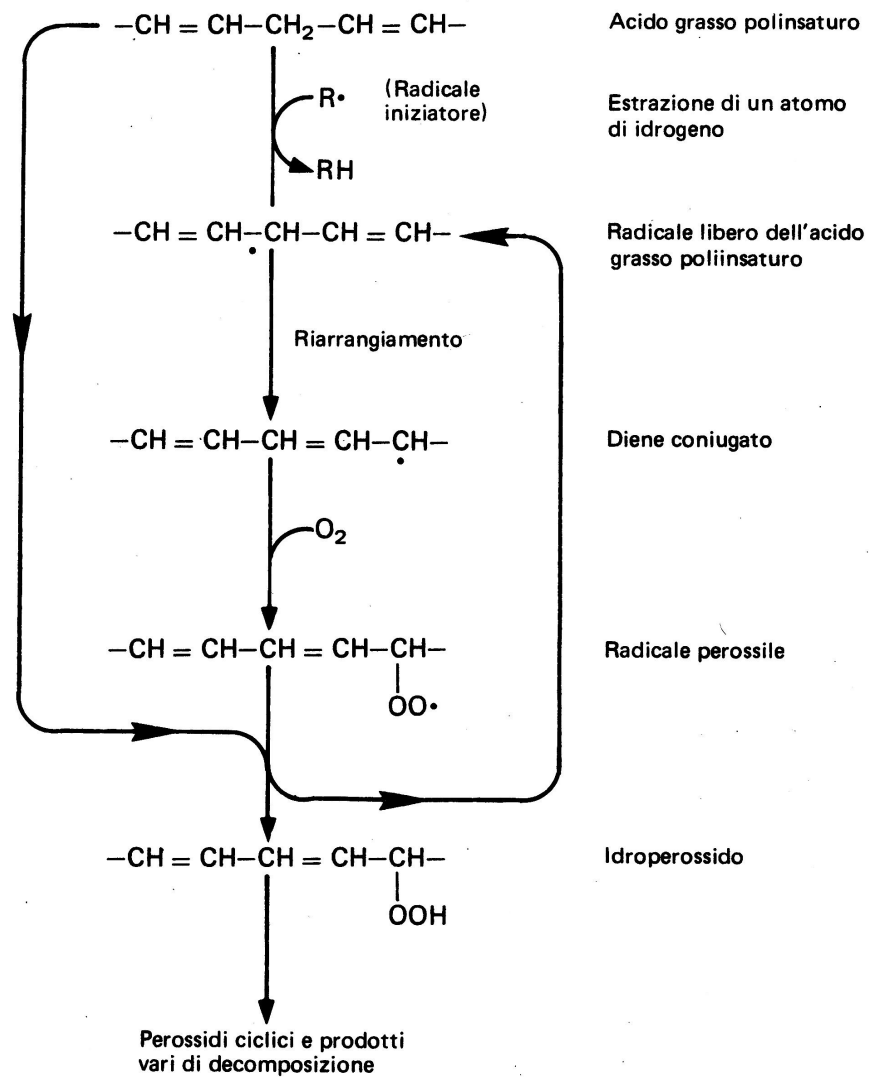
Fe-SOD

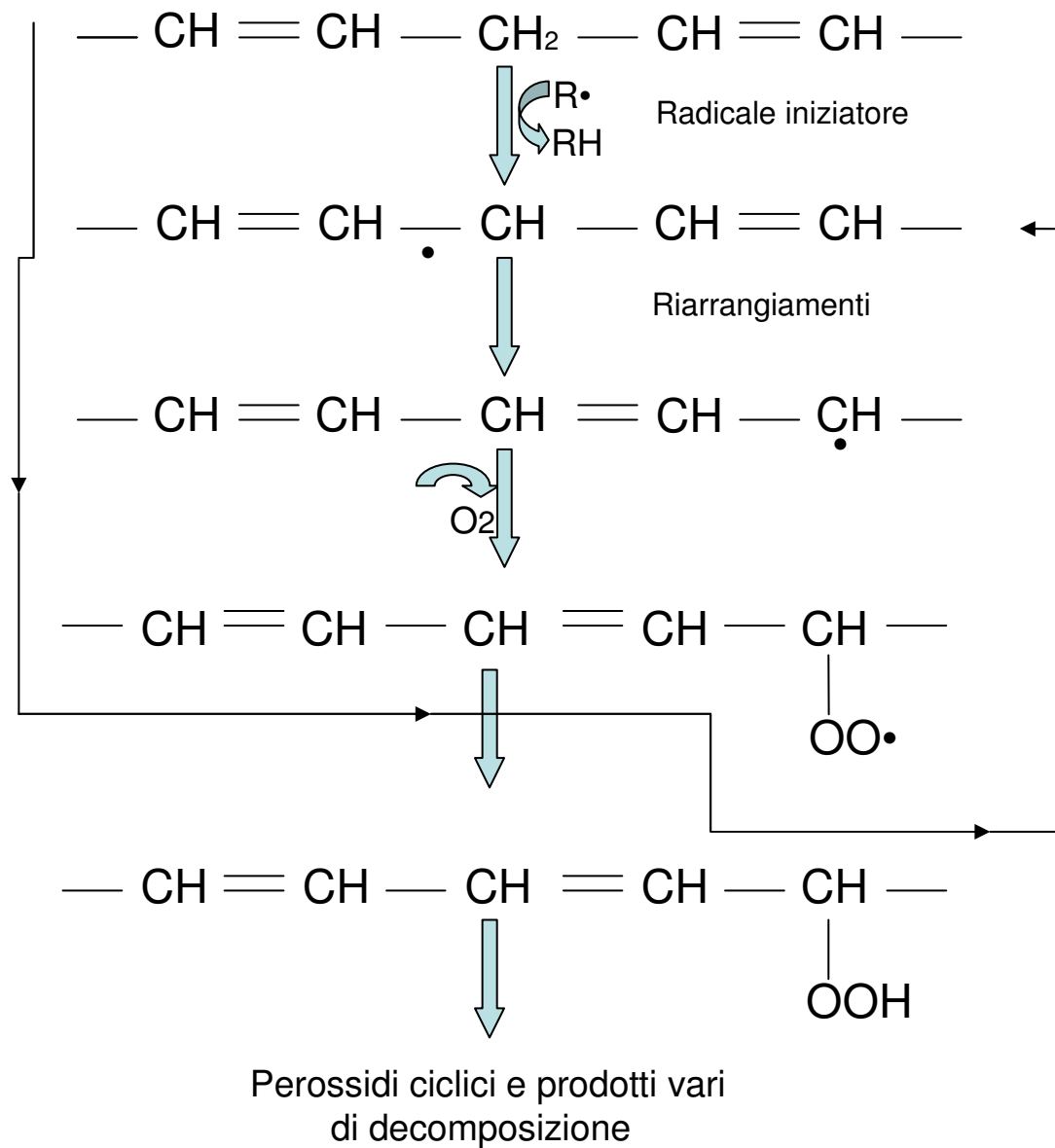


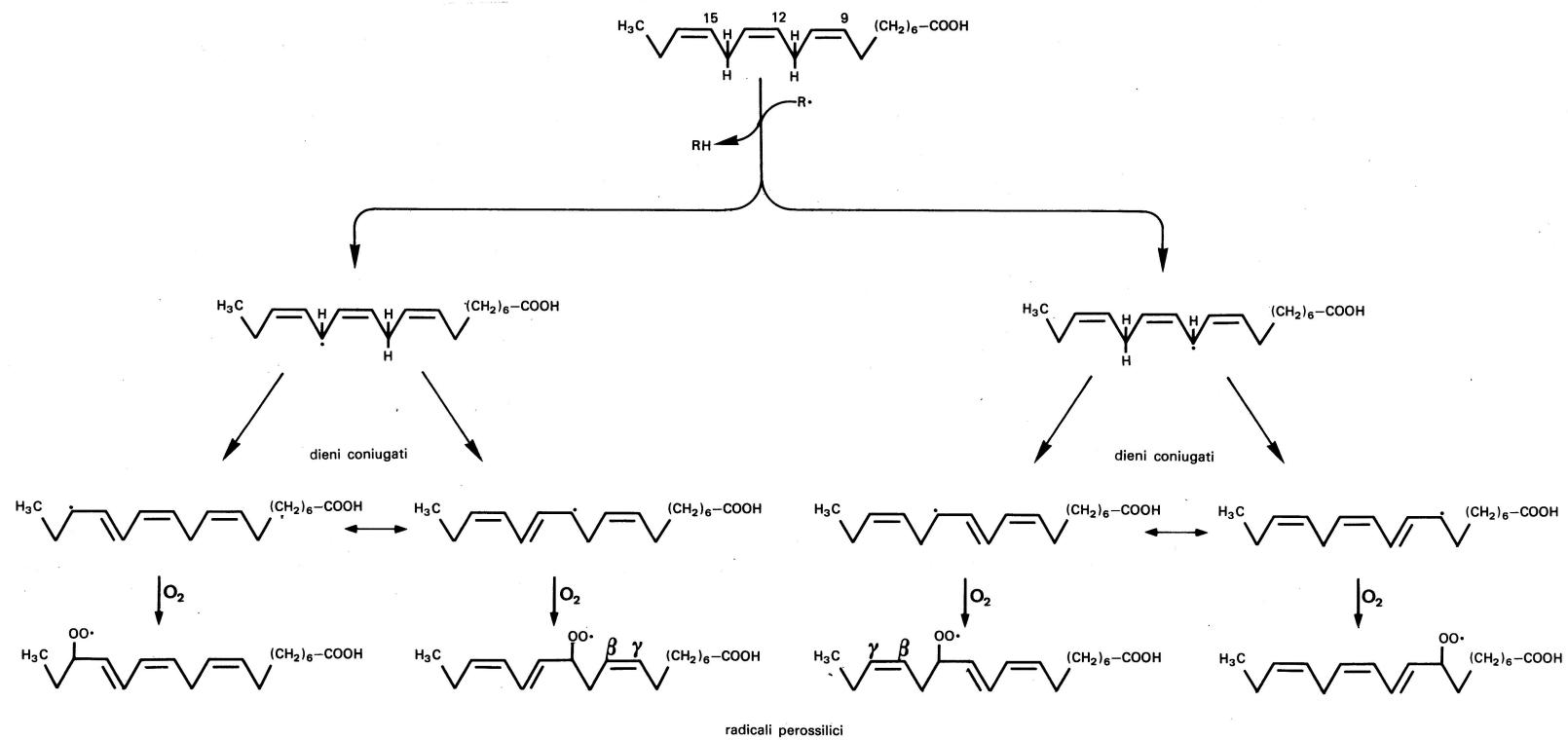
Ni-SOD



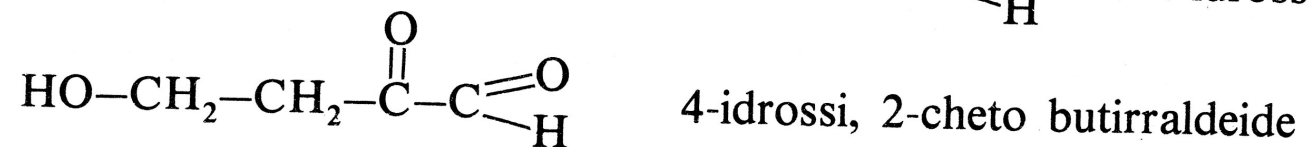
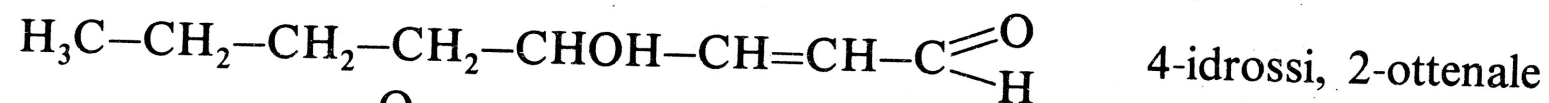
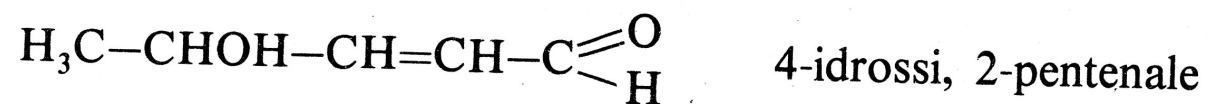
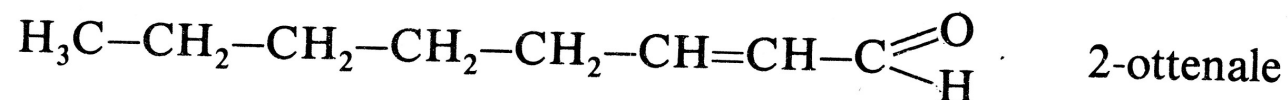
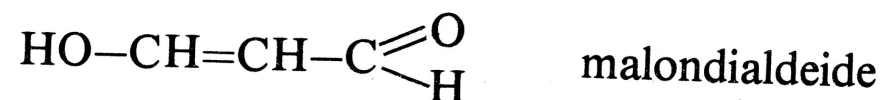




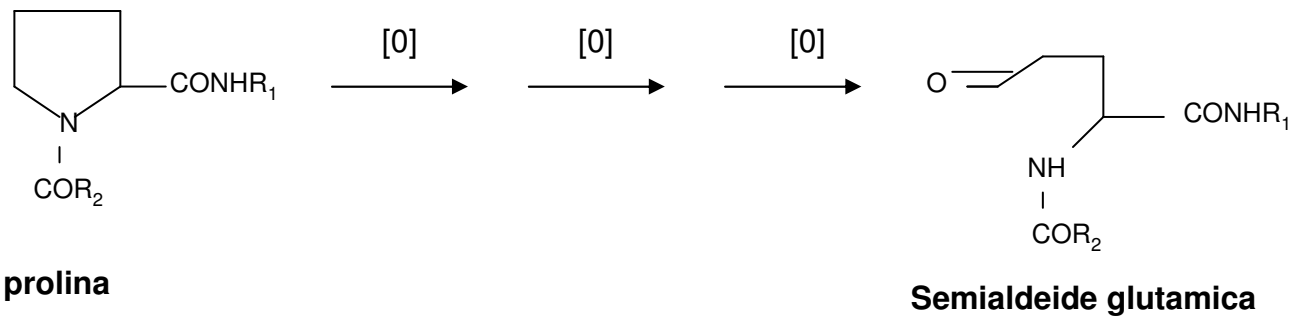




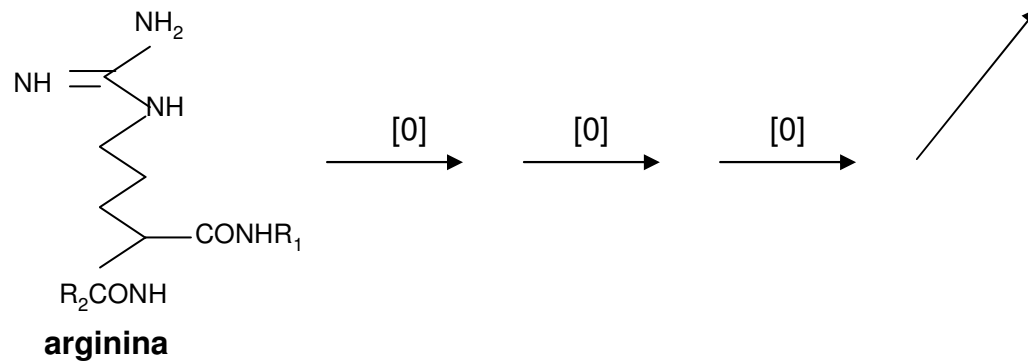
Prodotti di degradazione della perossidazione lipidica



a)



b)



c)

