Antioxidant action of two polyphenols, resveratrol and piceid, on a biological *in vitro* model

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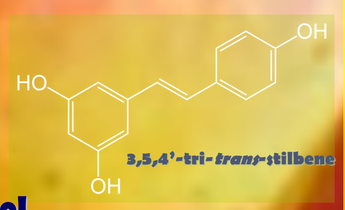
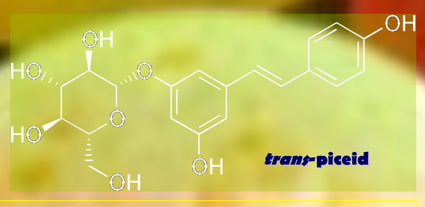
- ✓ UV
- ✓ fungal infection
- ✓ stress



***trans* - resveratrol**

- anticarcinogenic
- cardioprotective
- antioxidant

glucosilated resveratrol



- inhibition of lipid peroxidation through a protective long-time activity, particularly efficient at membrane
- scavenger action against radicals or radicalic initiators

French paradox

Low incidence of cardiovascular disease in France despite the high saturated fat daily intake. This has been attributed to the widespread consumption of wine containing polyphenols like resveratrol and piceid.

Introduction

Among natural antioxidants found in many natural foods and beverages, the flavonoid resveratrol and piceid have been proven to be effective against a broad range of diseases whose origin can be attributed to oxidative damage.

Resveratrol is a phytoalexin, a secondary metabolite synthesized by Spermatophytes in response to stress conditions caused, for example, by exposure to UV radiation or fungal infection. ***Piceid***, called also ***polidatina***, is the glucosylated form of resveratrol, and also shows two isomers ***cis*** and ***trans***; it is more resistant to enzymatic oxidation than resveratrol, enters the cell through an active transport mechanism that uses the glucose transporters, and, because of its higher solubility in water, is more efficiently absorbed from the mammal's intestine.

This work was planning to evaluate the antioxidant action of these polyphenols on a biological *in vitro* model (*i.e.* mitochondria) and to assess, then, any protective action of these stilbenes when the same organelle are exposed to toxic environmental substances well known to give rise to a state of oxidative stress. The choice of using a mitochondria-based bioassay was determined by the need to clarify the biochemical mechanisms underlying the antioxidant effect of resveratrol and piceid on natural membranes. In particular, starting from some studies [Fabris *et al.*, 2009] conducted to date on model membranes (*i.e.* synthetic organelles like micelles or liposomes), using ABIP as radicalic initiator, we tried to investigate resveratrol and piceid antioxidant action performed at mitochondrial membranes, using frozen beef heart mitochondria, called FM22 test [*see Poster TU 124 for more detailed information*].

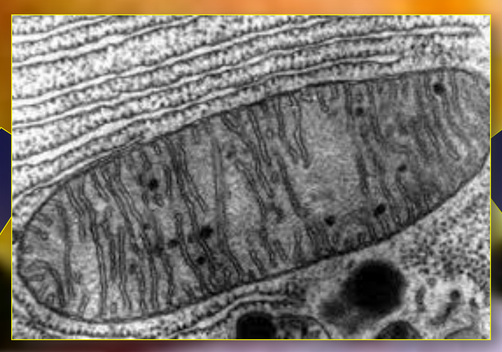
Initially, they has been utilized with the classical mitochondrial endpoint, *i.e.* respiratory chain inhibition [data not shown here]. Then, because it is reported that the antioxidant polyphenol's activity is linked to their ability to block or slow down lipid peroxidation, reacting with peroxy radicals formed in the propagation phase, we investigated the ability of resveratrol and piceid to interact with initiator radicals, since it is possible that oxidation is inhibited at the initiation stage. Indeed, the action of resveratrol and piceid as a scavenger against radical initiators and propagators of membrane oxidation, and its effectiveness in preventing the lipid peroxidation in different types of substrates, is well known.

Importance of exogenus antioxidants (resveratrol and piceid) uptake trough two different approaches testing natural, *i.e.* mitochondrial, membranes

I^st^ phase - Bibliografic search

Environmental compound identification able to produce oxidative stress

II^nd^ phase - Determination of concentration with lowest effect and testing effects in the presence of resveratrol and piceid



Monitoring the response of mitochondria in oxidative stress conditions a result of the radical initiator ABIP,

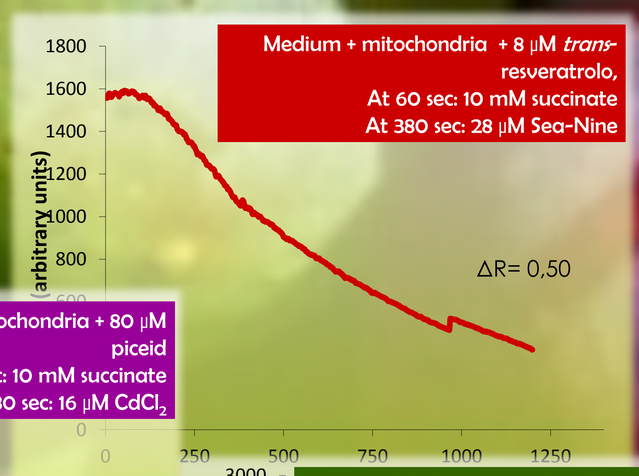
2,2'-azobis[2-2(imidazolin-2-yl)propane],

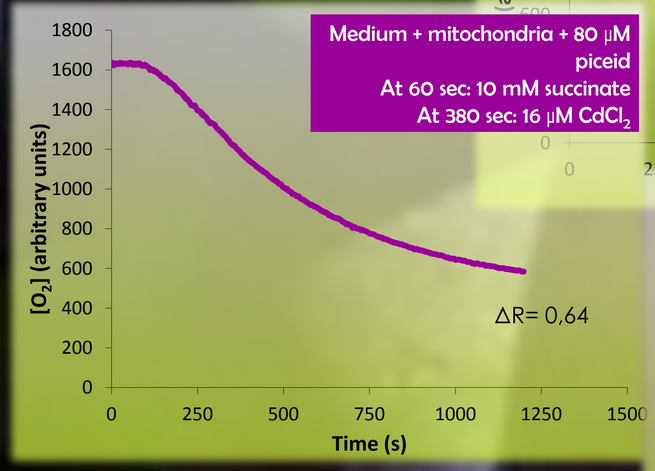
a well known lab's radicalic initiator

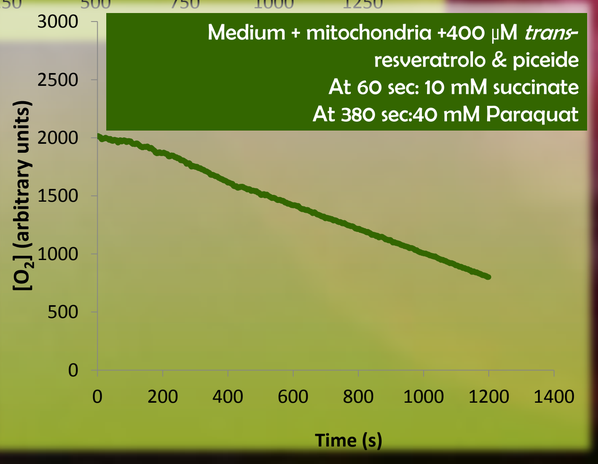
Sea-Nine®

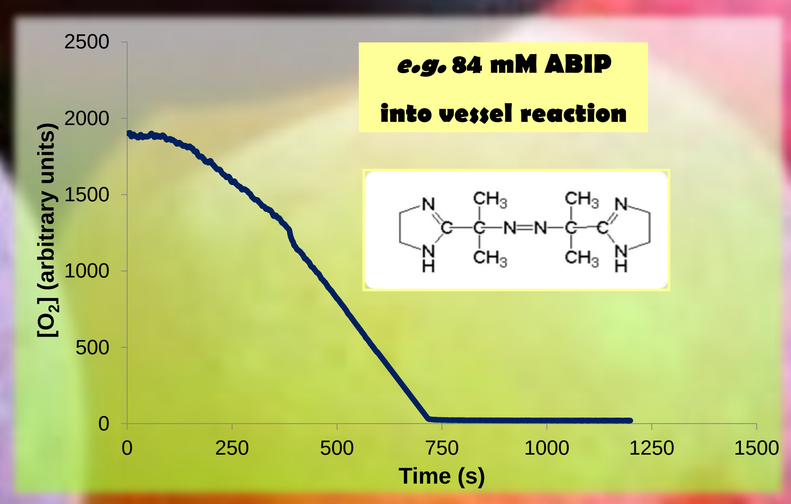
Cadmium

Paraquat









CONCLUSIONS

- **Objective limits of mitochondrial test because of organelle complexity; it is impossible to distinguish the specific action of tested antioxidant from other components of total mitochondrial output.**
- **Unable to shed light on the mitochondrial membrane antioxidant action of resveratrol and piceid demonstrated on synthetic membranes and to clarify their biochemical mechanisms on these membranes**
- **Trans-resveratrol and piceid not inhibit or have any unfavorable effect on the electron transport chain.**

general processes

radicalic initiator

$R\bullet + LH \rightarrow RH + L\bullet$

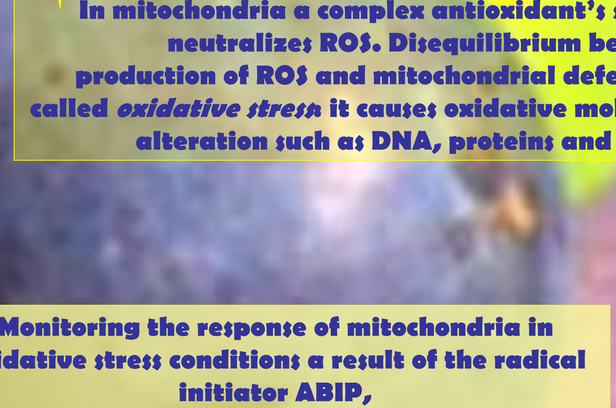
$L\bullet + O_2 \rightarrow LOO\bullet$ → **radicalic propagator**

$LOO\bullet + LH \rightarrow LOOH + L\bullet$

$L\bullet + O_2 \rightarrow LOO\bullet$

$L\bullet / LOO\bullet \rightarrow$ **non radical product**

lipidic peroxidation



oxidant species

- **from exogenous source**
- **from aerobic metabolism**

Reactive Oxygen Species (ROS)

Oxidative stress

Mitochondrial respiratory chain is one of the major sources of endogenous ROS because the continuous cycle of oxidation / reduction of electron carriers results in several side reactions with molecular oxygen.

In mitochondria a complex antioxidant's system neutralizes ROS. Disequilibrium between production of ROS and mitochondrial defences is called *oxidative stress*: it causes oxidative molecules alteration such as DNA, proteins and lipids.

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KEYWORDS
Antioxidant
Resveratrol
Mitochondria
Lipid peroxidation