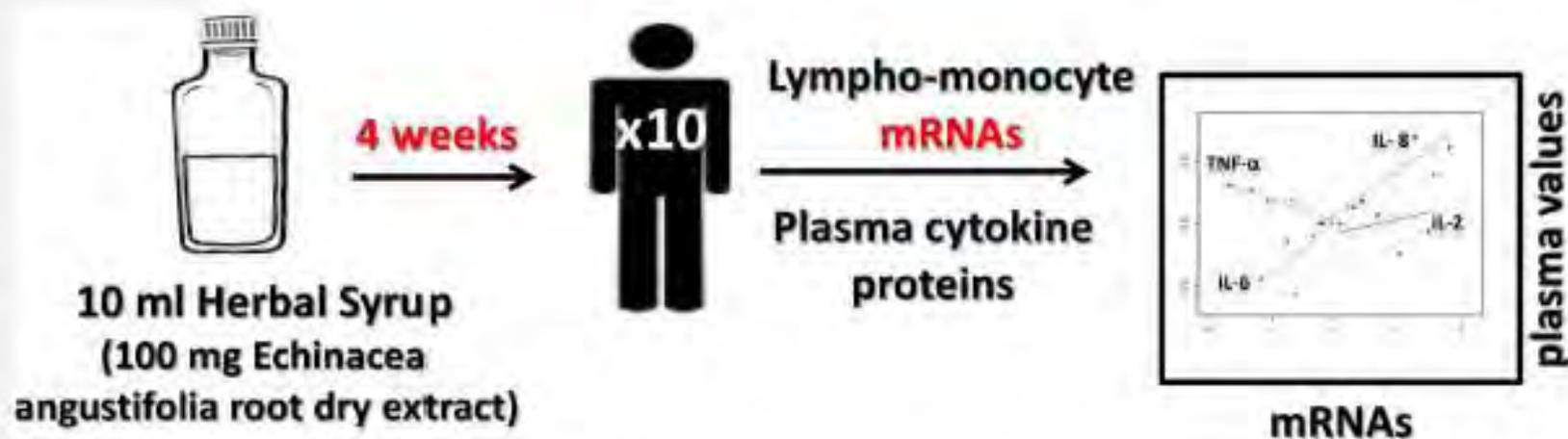




Immunomodulation mediated by a herbal syrup containing a standardized Echinacea root extract: A pilot study in healthy human subjects on cytokine gene expression



B. Dapas^a, S. Dall'Acqua^b, R. Bulla^c, C. Agostinis^{c,d}, B. Perissutti^e, S. Invernizzi^c, G. Grassi^a, D. Voinovich^{c,*}



corresponding to 4.7 mg of Echinacoside and 8.0 mg of a high molecular weight-20,000 Da- polysaccharide

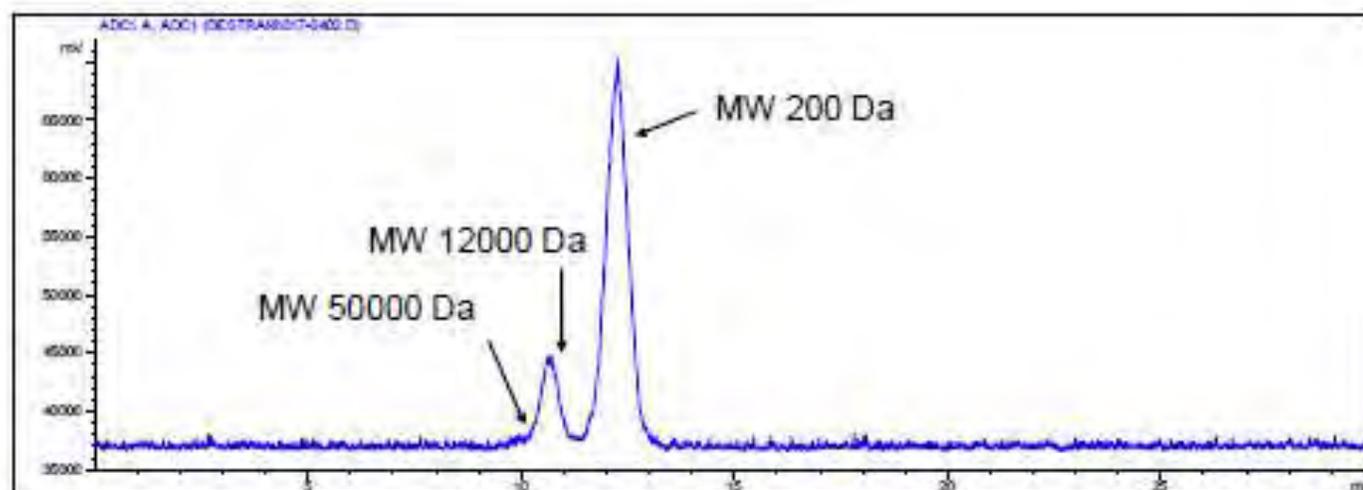


Fig. S2. Chromatogram obtained with ELSD detector, showing the polysaccharides.

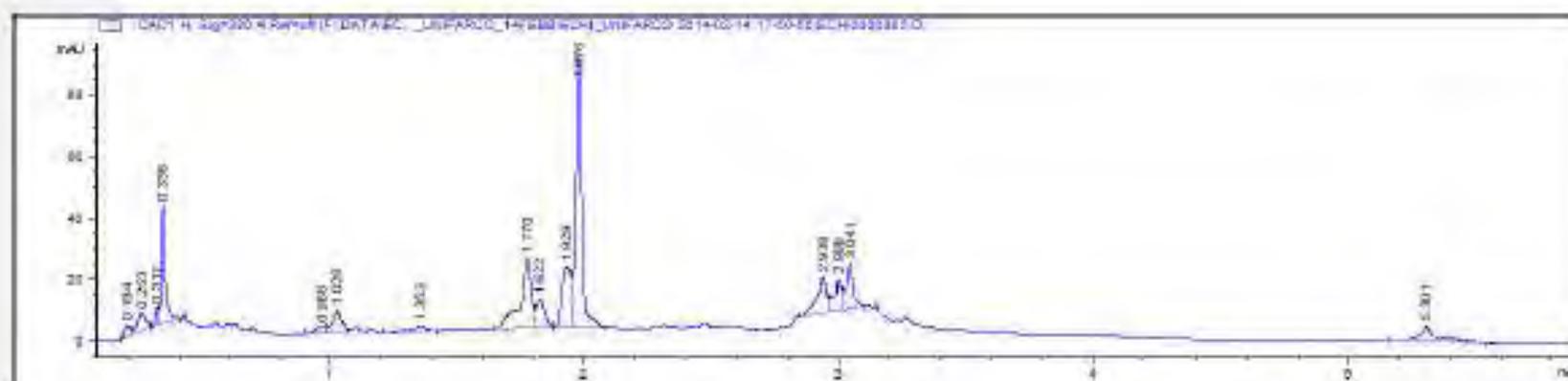


Fig. S1. Chromatogram of the syrup obtained by DAD detector at 330 nm, showing echinacoside peak at 1.98 minutes.

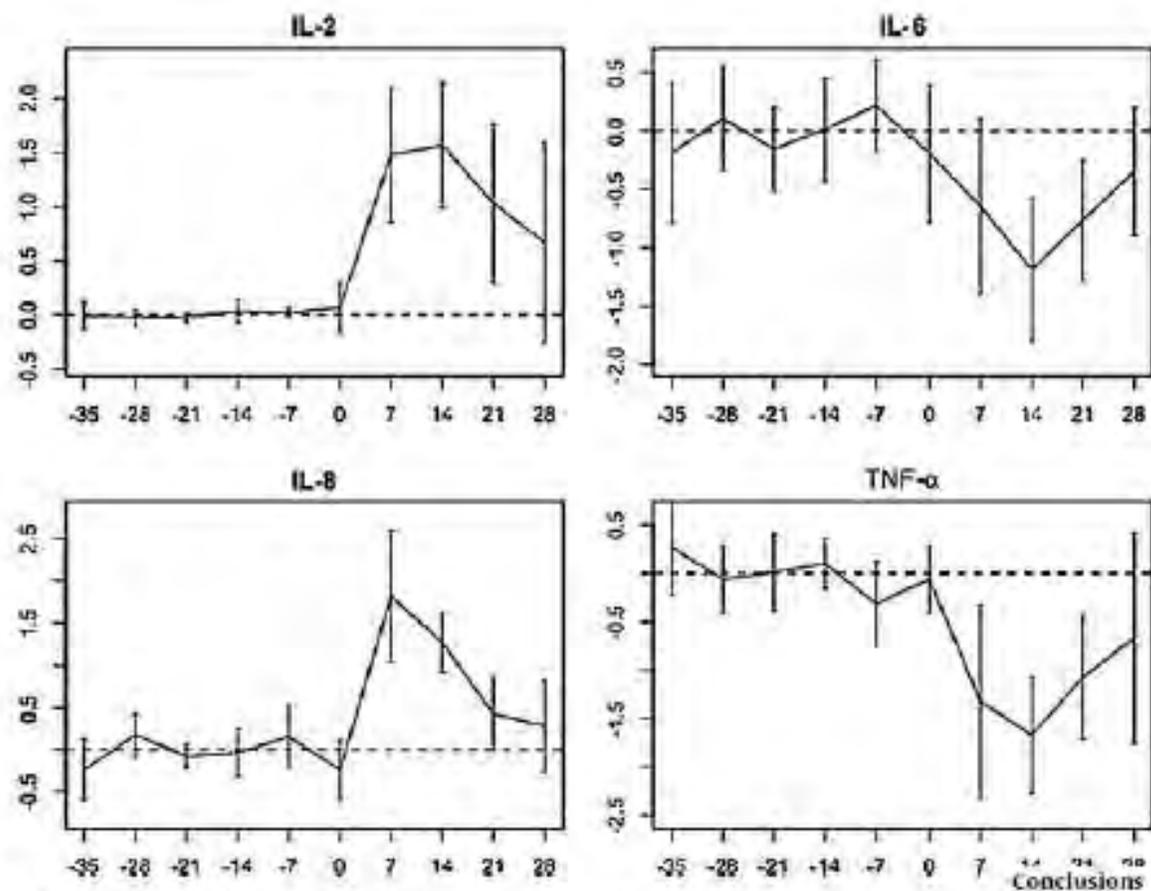


Fig. 1. Plot of mean (±S.D.) differences of mRNA values with respect to pre-treatment values (initial baseline) are represented.

In this pilot study, 10 human volunteers have been treated for four weeks with a herbal syrup product containing 100 mg of *Polinacea*[®] (corresponding to 4.7 mg of Echinacoside and 8.0 mg of high molecular weight polysaccharide). Limitations of this study include the small size of the sample population and the lack of comparison with other *Echinacea* extracts with different composition. Despite this, the presented data suggests possible mechanisms by which the formulated syrup influences the immune system functions, in particular via the down regulation of IL-6 expression. Additionally this study demonstrates the immuno-modulating activity of *Polinacea*[®] in the healthy subject, supporting at least in part its use as health promoting supplement. Future perspectives include a systematic study in a larger trial, the inclusion of cold affected individuals and the effects of seasonality.



Original Article

Combined extracts of *Echinacea angustifolia* DC. and *Zingiber officinale* Roscoe in softgel capsules: Pharmacokinetics and immunomodulatory effects assessed by gene expression profiling

Stefano Dall'Acqua^a, Iztok Grabnar^b, Roberto Verardo^c, Enio Klaric^c, Luigi Marchionni^d, Eddie Luidy-Imada^{d,e}, Stefania Sur^f, Chiara Agostinis^g, Roberta Bulla^h, Beatrice Perissutti^f, Dario Voinovich^h

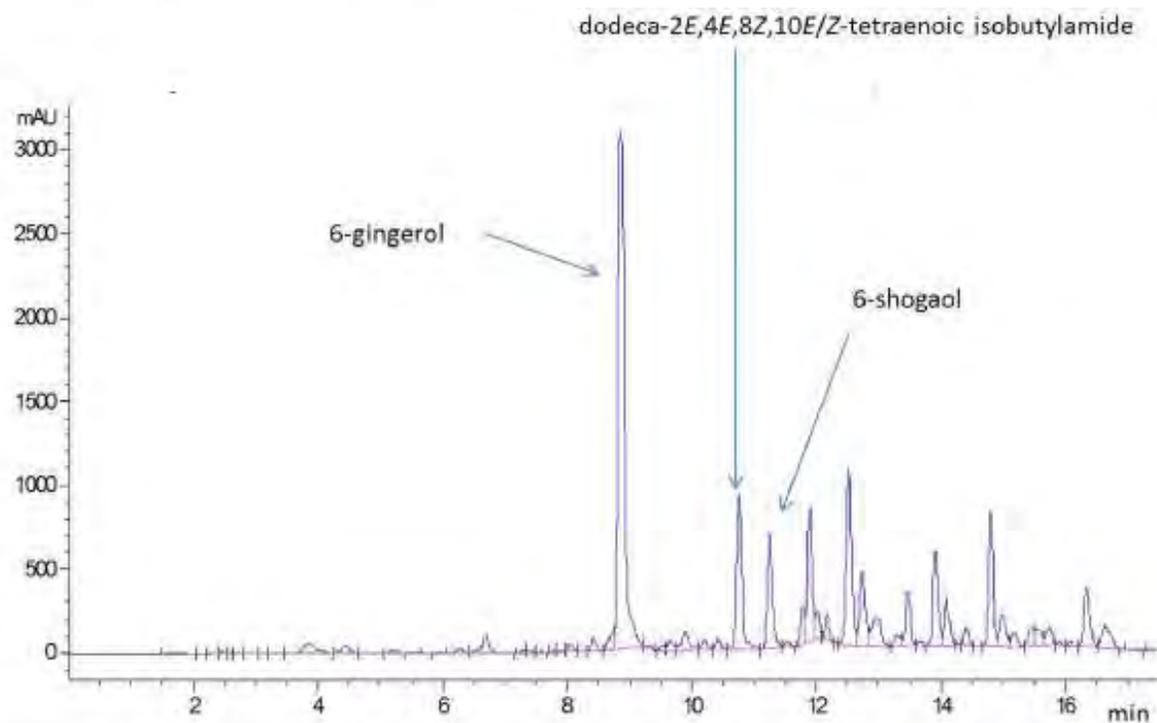


Fig. 1. Representative HPLC-DAD chromatogram of the used product; peaks assigned to the active constituents highlighted in the study are reported.

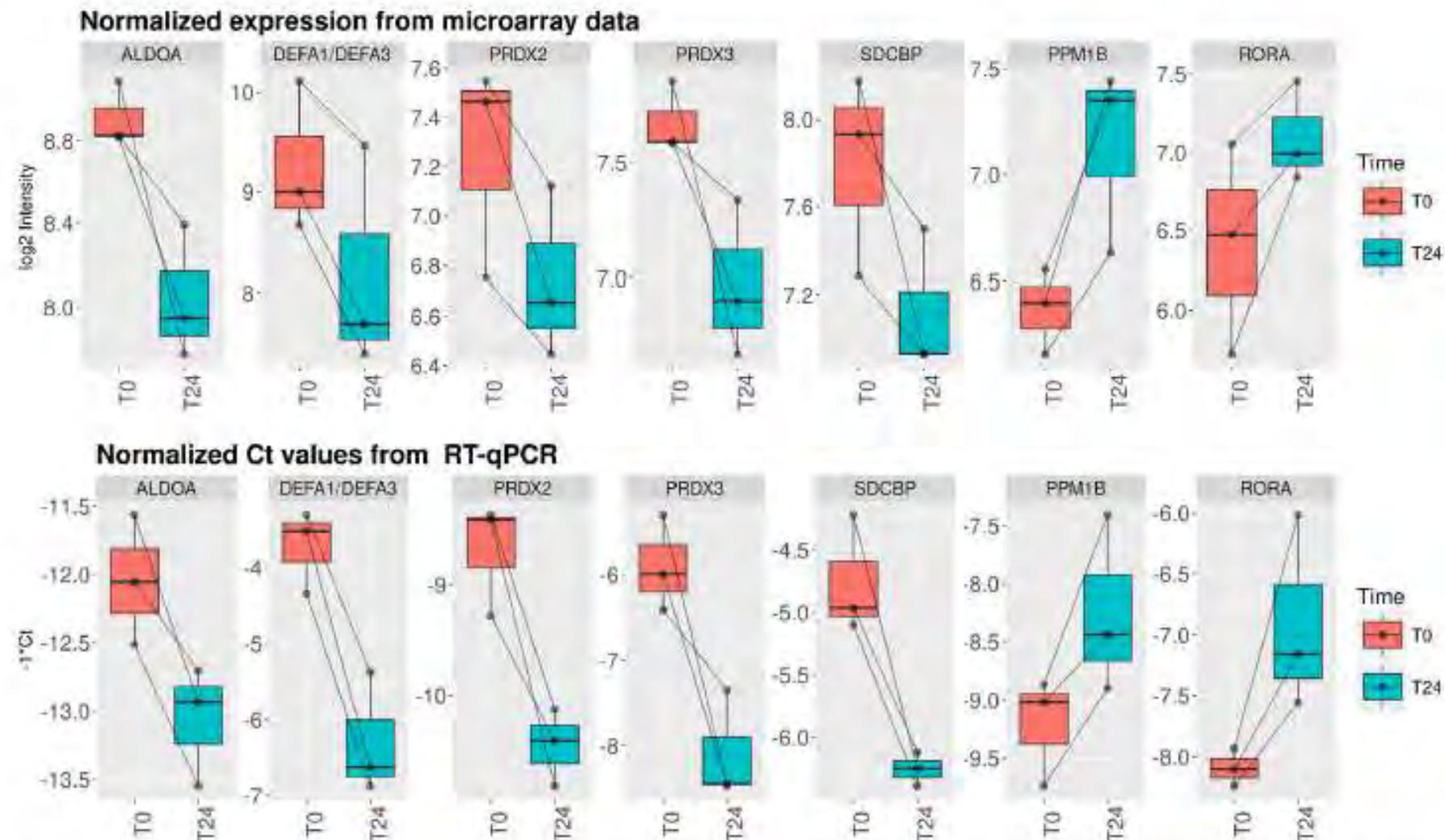


Fig. 3. Validation of selected genes differentially expressed following administration of the lipophilic extracts at two distinct time points (T0 and T24). Boxplots show expression levels change between paired samples (3 distinct donors) analyzed by microarray (Upper Panel) and by RT-qPCR (Lower Panel). Expression levels are expressed as normalized \log_2 expression intensities for microarrays and as normalized (to ACTB housekeeping gene) Ct values for RT-qPCR. Individual matching T0 and T24 measurements for each donor are connected. Our validation experiments confirmed that ALDOA, DEFA1/DEFA3, PRDX2, PRDX3, and SDCBP are down-regulated upon treatment, while PPM1B and RORA are up-regulated. Primers pairs used for RT-qPCR are listed in Table S2).

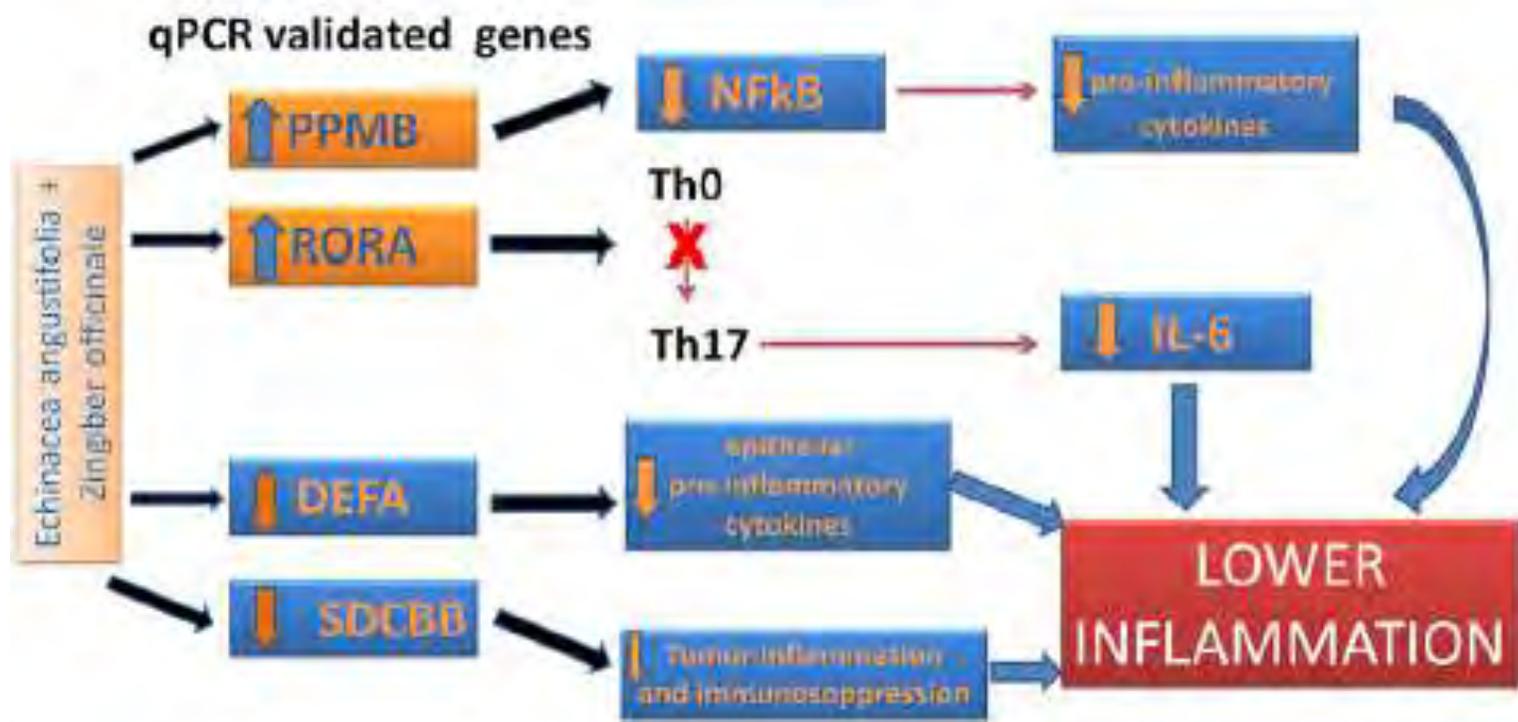


Fig. 6. Modulation concurring to shift the leukocytes towards an anti-inflammatory phenotype.

Migliore assorbimento e farmacocinetica
 Azione immunomodulatoria
 Azione antinfiammatoria

Precauzioni per CYP

Molteplici meccanismi
d'azione

Importanza
standardizzazione



Allergie?
Reazioni di
sensibilizzazione
(asteraceae)

Generalmente ben
tollerata

Importanza
formulazione

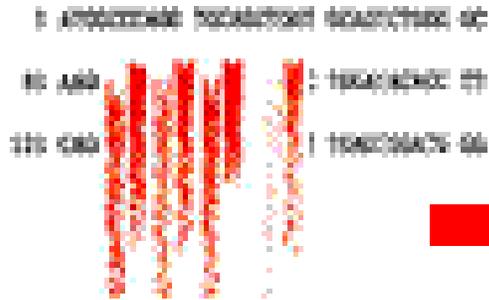
Dosi e durata dei
trattamenti

Consiglio sia in prevenzione per stimolare le difese immunitarie

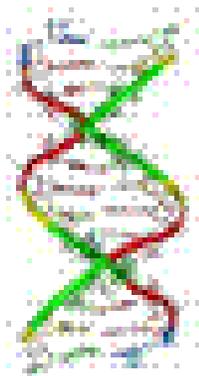
Sia in acuto per migliorare la risposta e sfruttare le azioni sulle citochine antiinfiammatorie

Associabile a vitamina C

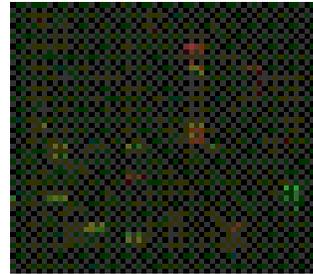
Associazioni con



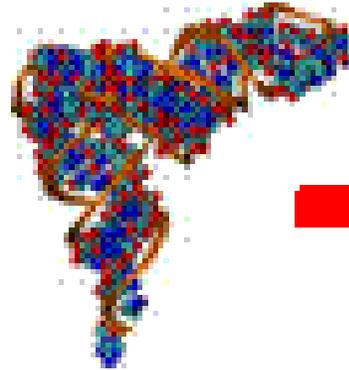
Genomics



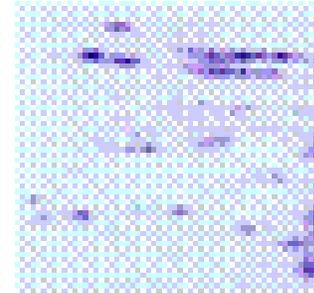
DNA



Transcriptomics



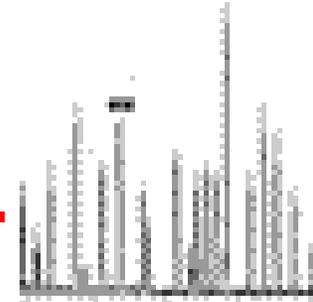
RNA



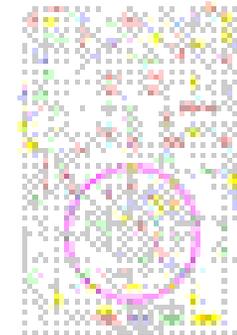
Proteomics



Protein

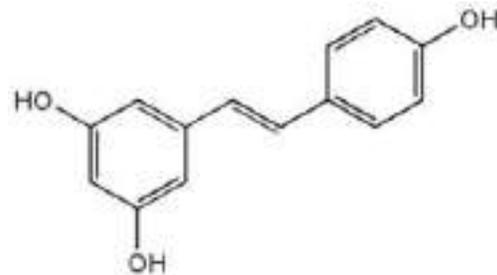


Metabolomics



Metabolites

Japanese knotweed (*Polygonum cuspidatum* Sieb. et Zucc.)



Contents lists available at [ScienceDirect](#)

Journal of Pharmaceutical and Biomedical Analysis

journal homepage: www.elsevier.com/locate/jpba



Studying the effects of natural extracts with metabolomics: A longitudinal study on the supplementation of healthy rats with *Polygonum cuspidatum* Sieb. et Zucc.



Gregorio Peron^{a,1}, Jalal Uddin^{b,1}, Matteo Stocchero^c, Stefano Mammi^b,
Elisabetta Schievano^b, Stefano Dall'Acqua^{a,*}

^a Department of Pharmaceutical and Pharmacological Sciences, University of Padova, Via Marzolo 5, 35131 Padova, Italy

^b Department of Chemical Sciences, University of Padova, Via Marzolo 1, 35131 Padova, Italy

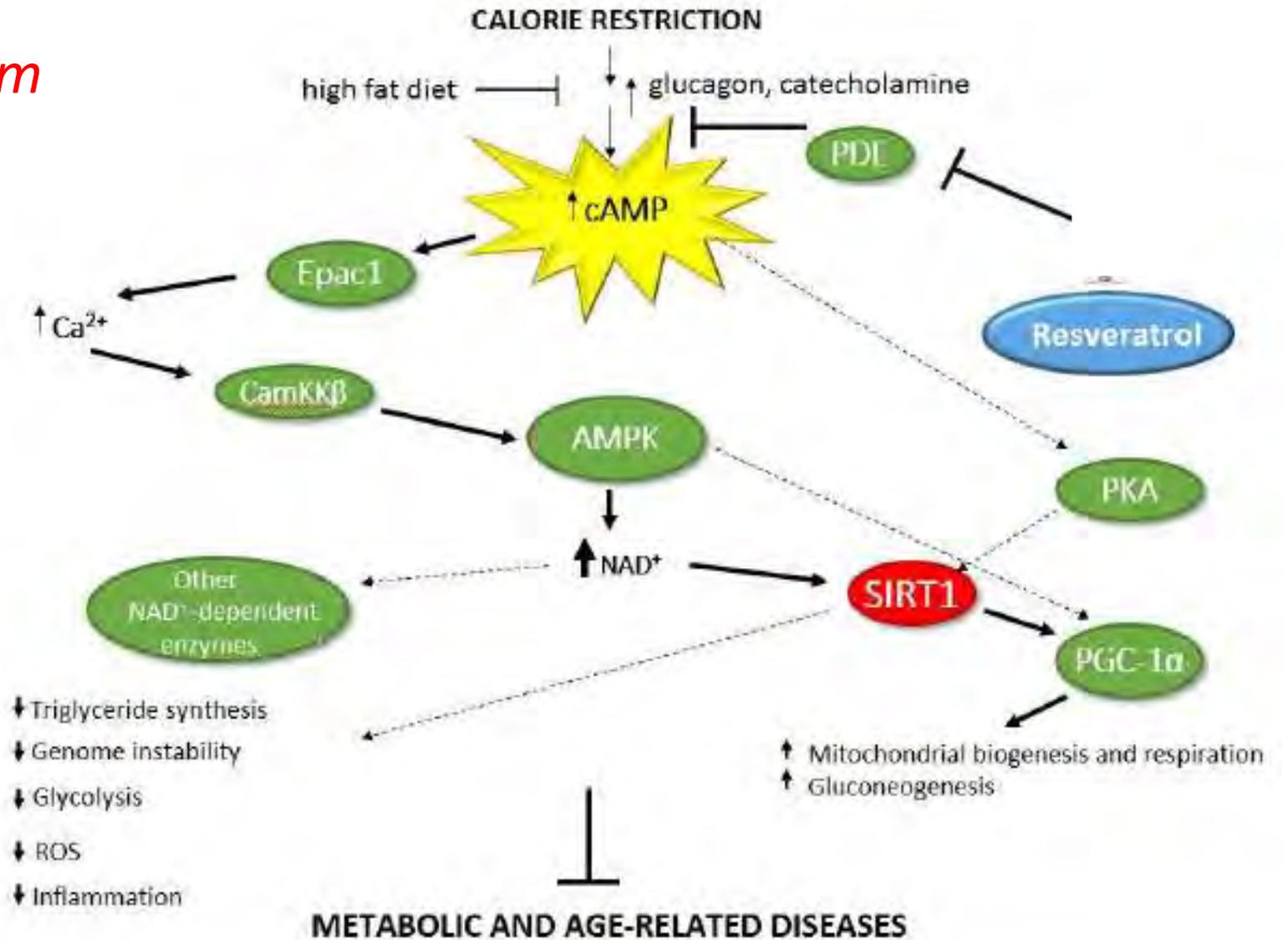
^c S-IN Soluzioni Informatiche, Via Ferrari 14, 36100 Vicenza, Italy

1222-2022
800
ANNI



UNIVERSITÀ
DEGLI STUDI
DI PADOVA

Polygonum cuspidatum



Resveratrol mode of action is not yet clear.

Resveratrol act through multiple targets



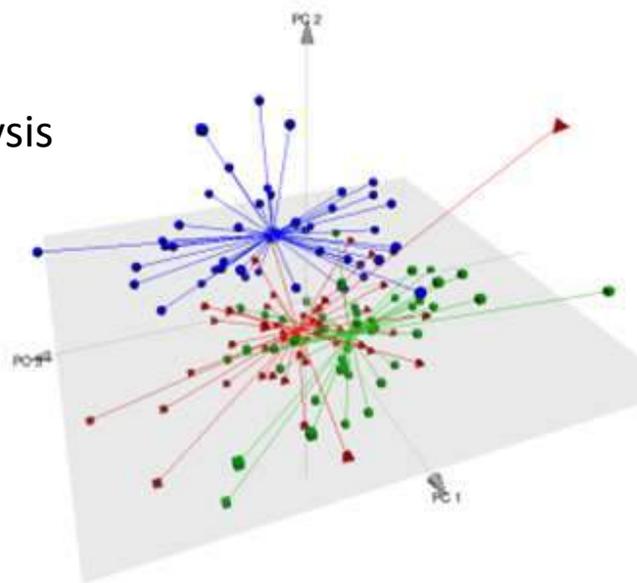
24h collection

1222-2022
800
ANNI

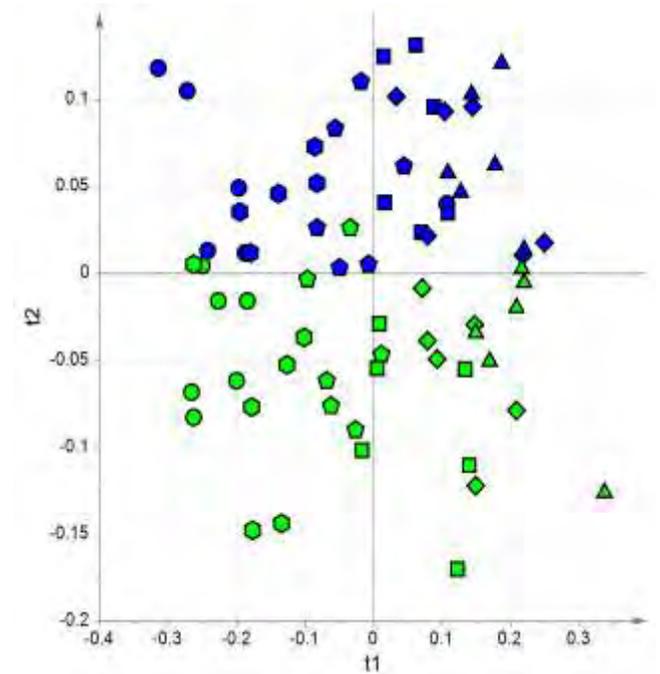


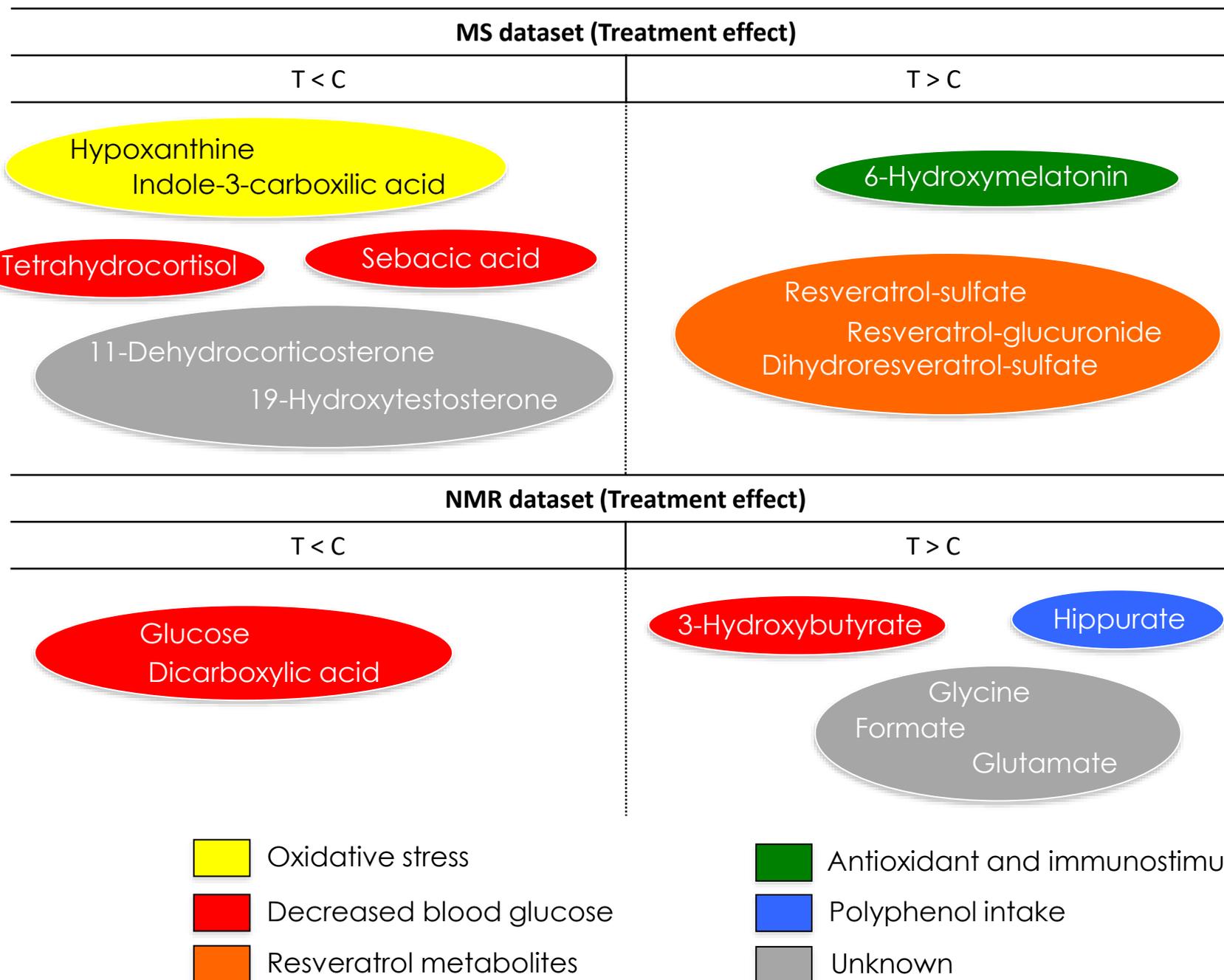
UNIVERSITÀ
DEGLI STUDI
DI PADOVA

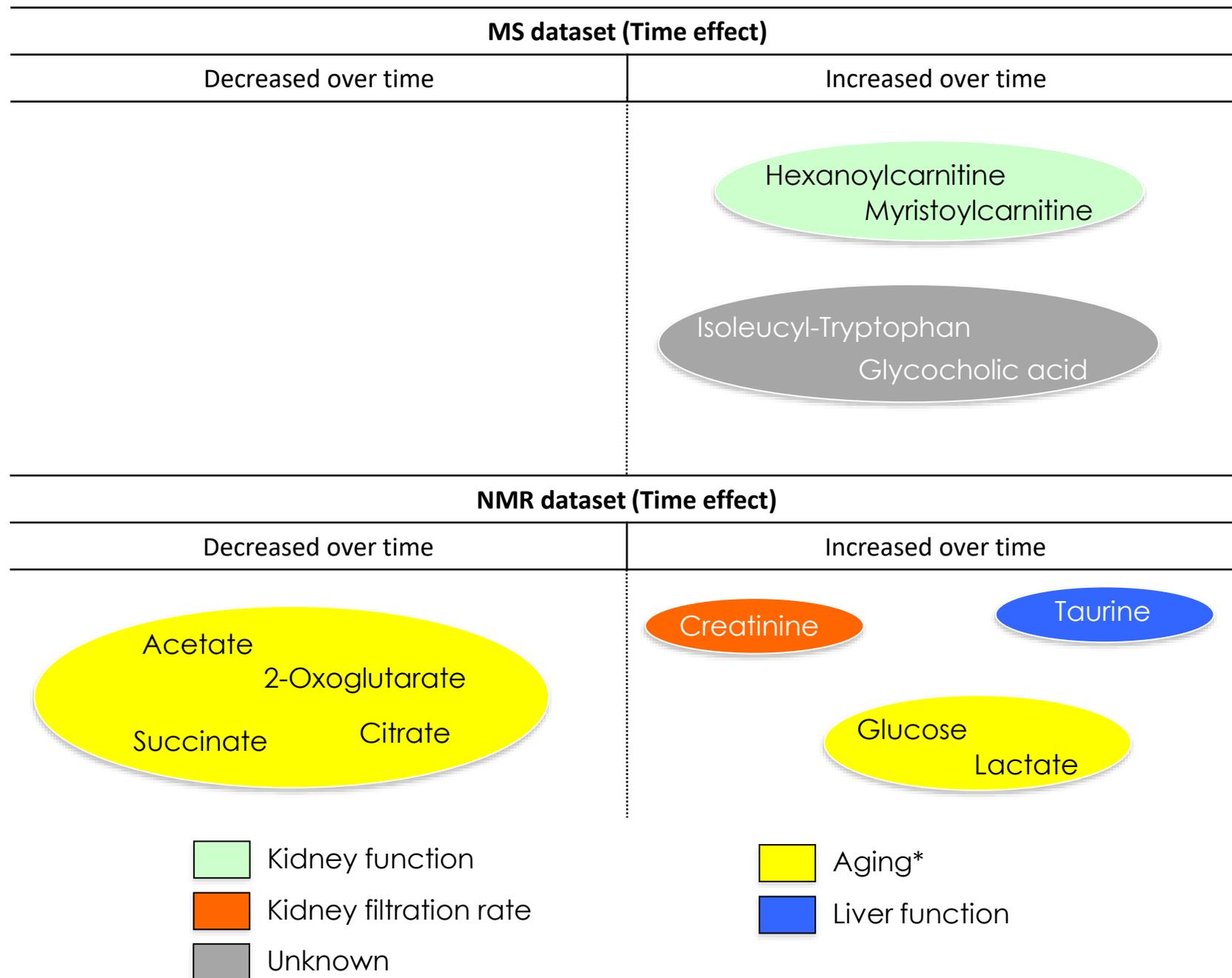
Untargeted UPLC-QTOF analysis



H-NMR analysis

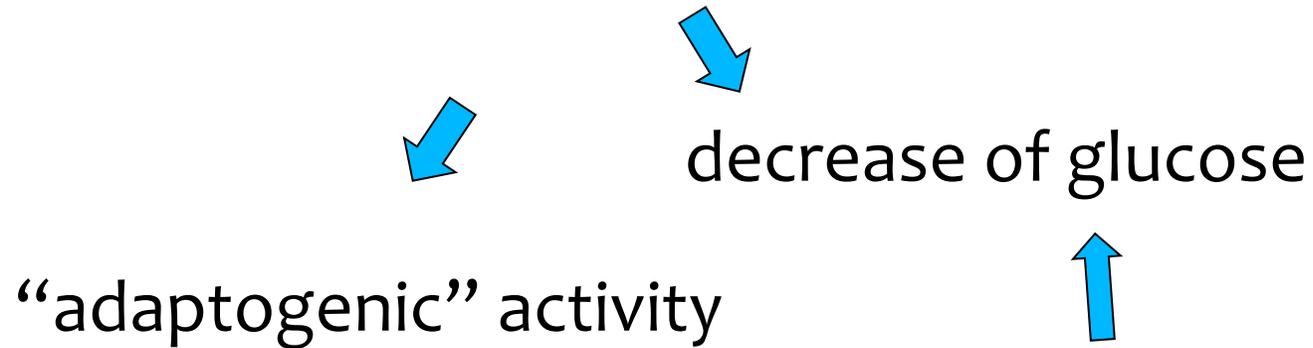






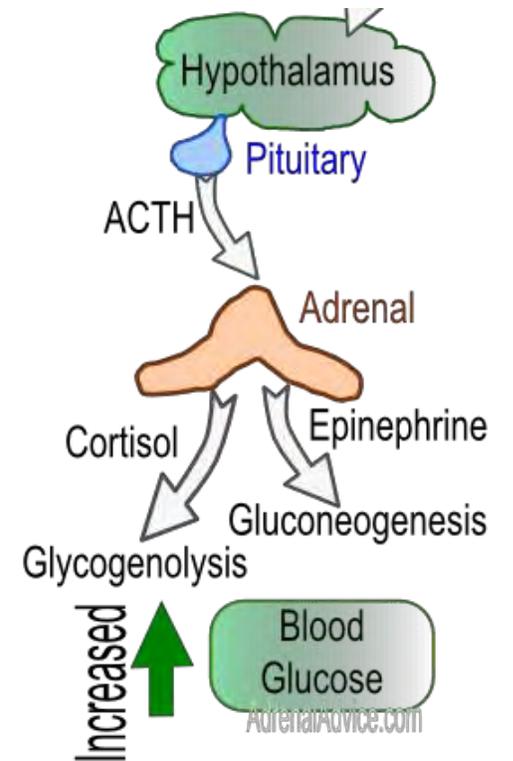
Possible mode of action on «starvation effect»

P. cuspidatum decreased tetrahydrocortisol urinary levels



CONFIRMED BY H-NMR DATA

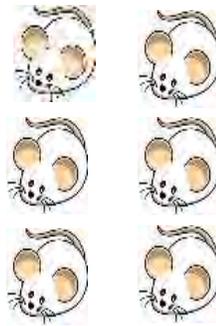
Increase of 3 hydroxybutyrate
(indication of starvation)



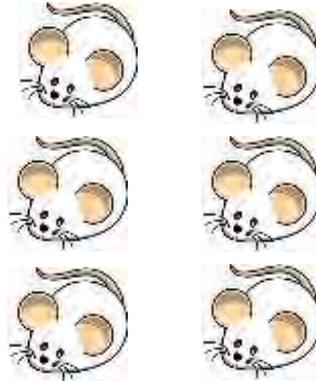


P.cuspidatum
Extract or
control

Day 0



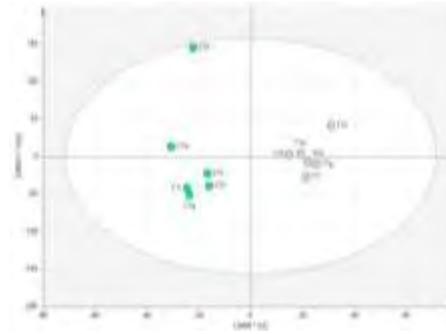
Day
49



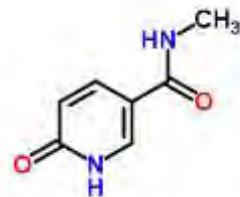
URINE
COLLECTION

UPLC-MS

METABOLOMIC

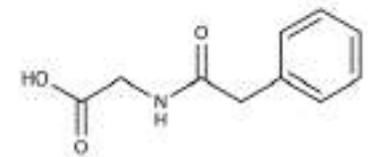


CHANGES IN AGEING MARKERS



2PY

PAG

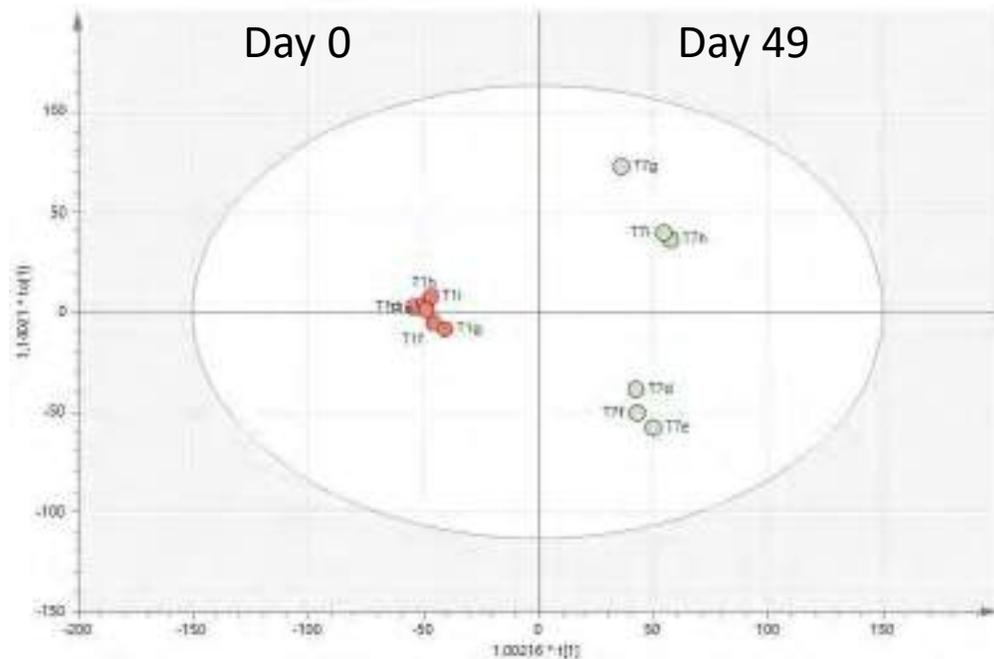
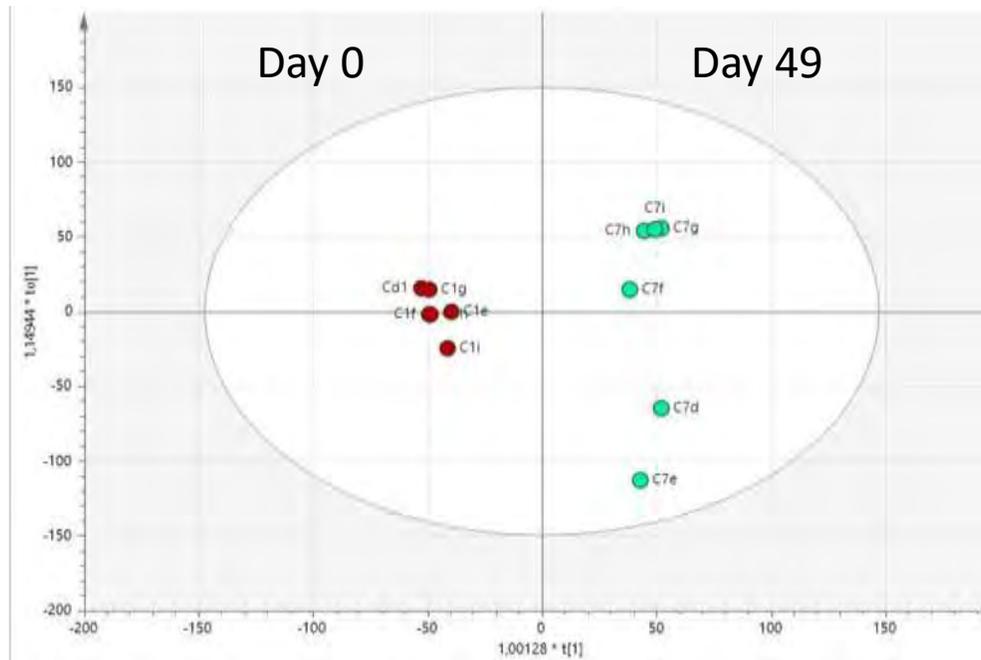


Supplementation with resveratrol as *Polygonum cuspidatum* Sieb. et Zucc. extract induces changes in the excretion of urinary markers associated to aging in rats

Gregorio Peron^a, Stefano Dall'Acqua^{b,*}, Stefania Sut^b

^a USP Department of Pharmaceutical and Pharmacological Sciences, University of Padova, via Marzolo 5, 35121 Padova, Italy

^b DAFNAB, Department of Agronomy Animal Food, Natural Resources and Environment, Viale dell'Università, 16, 35020 Legnaro, University of Padova.

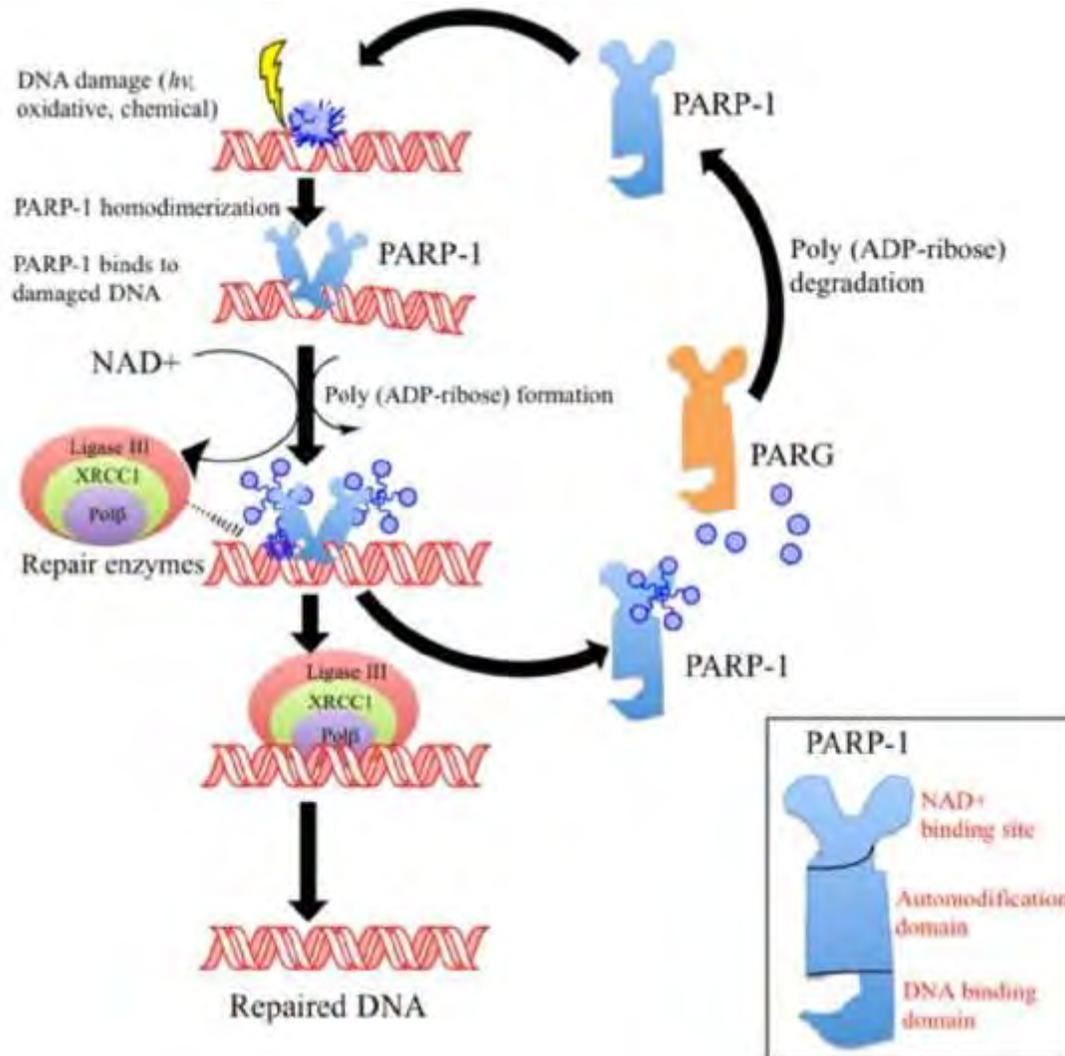


Treated group

Metabolomic analysis of urine samples allowed the observation of differences due to ageing and/or treatment



Results: effects of *P. cuspidatum* on aging

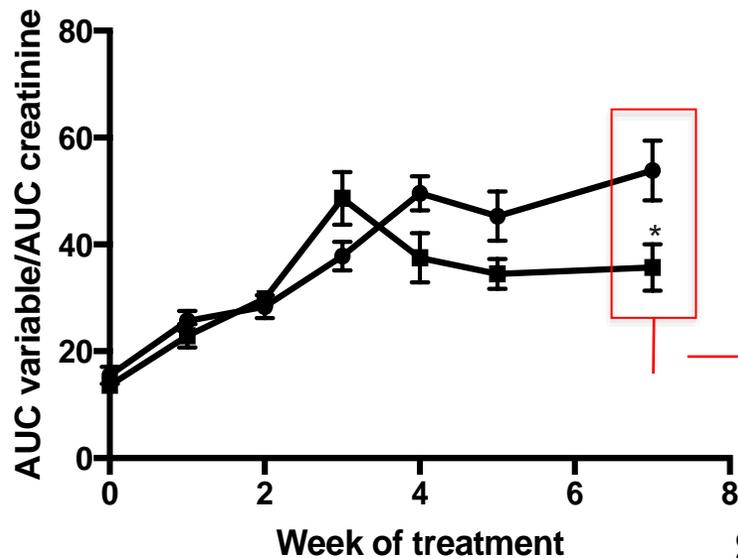


2PY

Metabolite of NAD

- ↑ ROS with aging
- ROS damage DNA
- PARP-1 enzyme induced
- ↑ Production of 2PY

↓
Marker of aging



N-methyl-2-pyridone-5-carboxamide (2PY)

- Control group
- Treated group

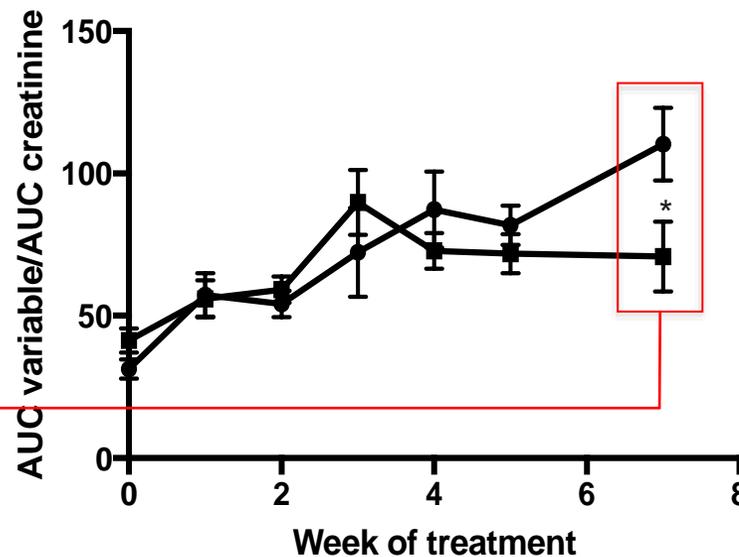
C = 53.8
T = 35.7

↓ **33.6%**

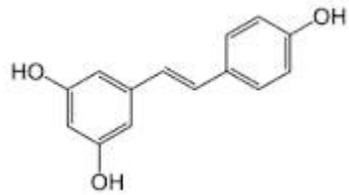
Phenylacetyl glycine

↓ **35.8%**

C = 110.3
T = 70.8



- Control group
- Treated group



**DECREASE OF URINARY
MARKERS OF
OXIDATIVE STRESS**

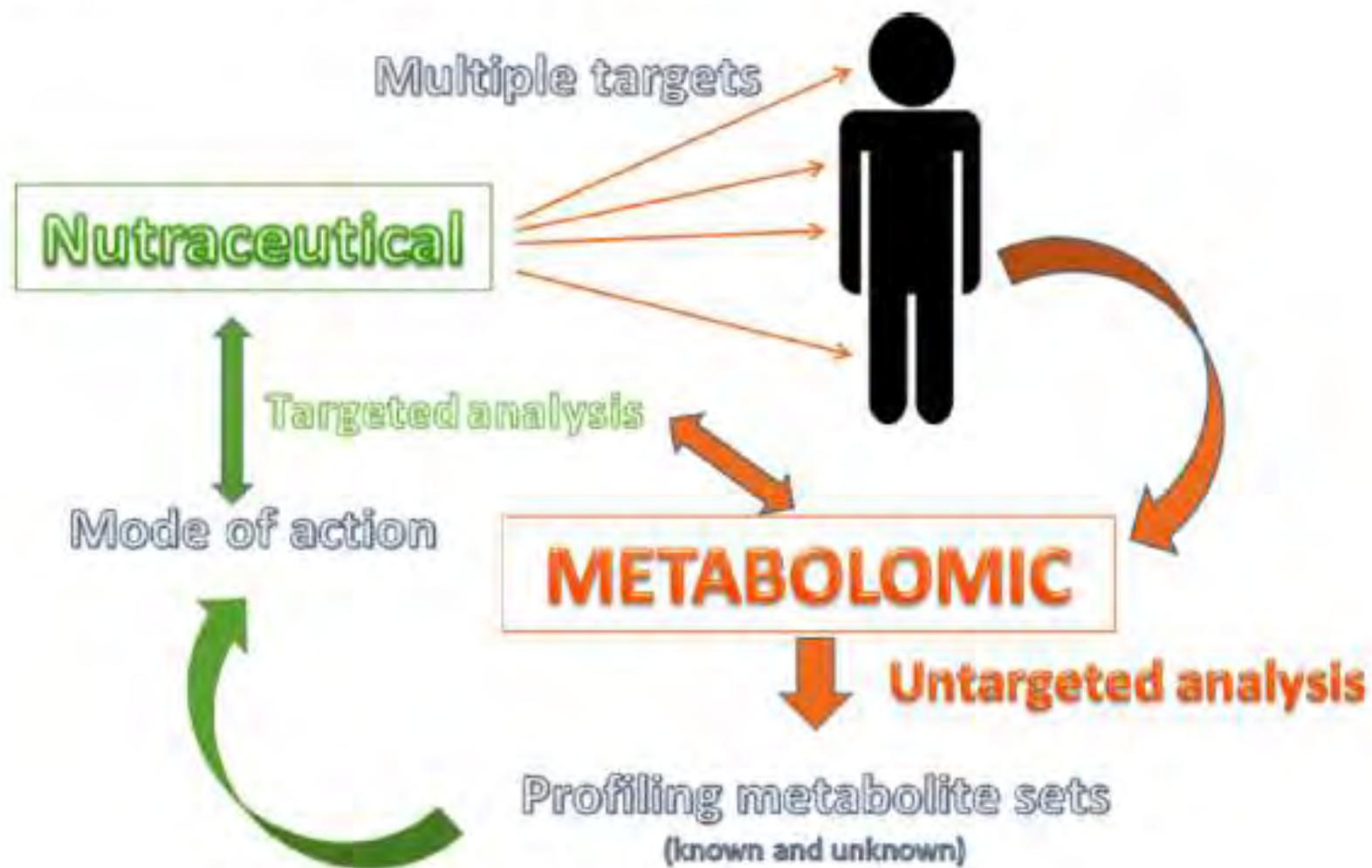


**CHANGES TO
ENERGY-RELATED
METABOLITES**



**CHANGES TO
TETRAHYDROCORTISOL
URINARY LEVELS**

Possible model for exploring age
related modifications to
metabolites



Picnogenolo

- Estratto brevettato da pinus pinaster
- Composizione ben caratterizzata e standardizzata
- Ricco in procianidine di tipo B, taxifolina
- Molti studi a supporto

Table 1

Representative constituents and percentages of pine bark extract as determined by HPLC analysis.

Constituent Percentage

Galic acid 3.2

Dimers (catechin and epicatechin) 40.9

Catechin **a** 18.9

Pic X **b** 12.8

Cafeic acid **a** 1.9

Epicatechin 0.2

Coumaric acid 0.2

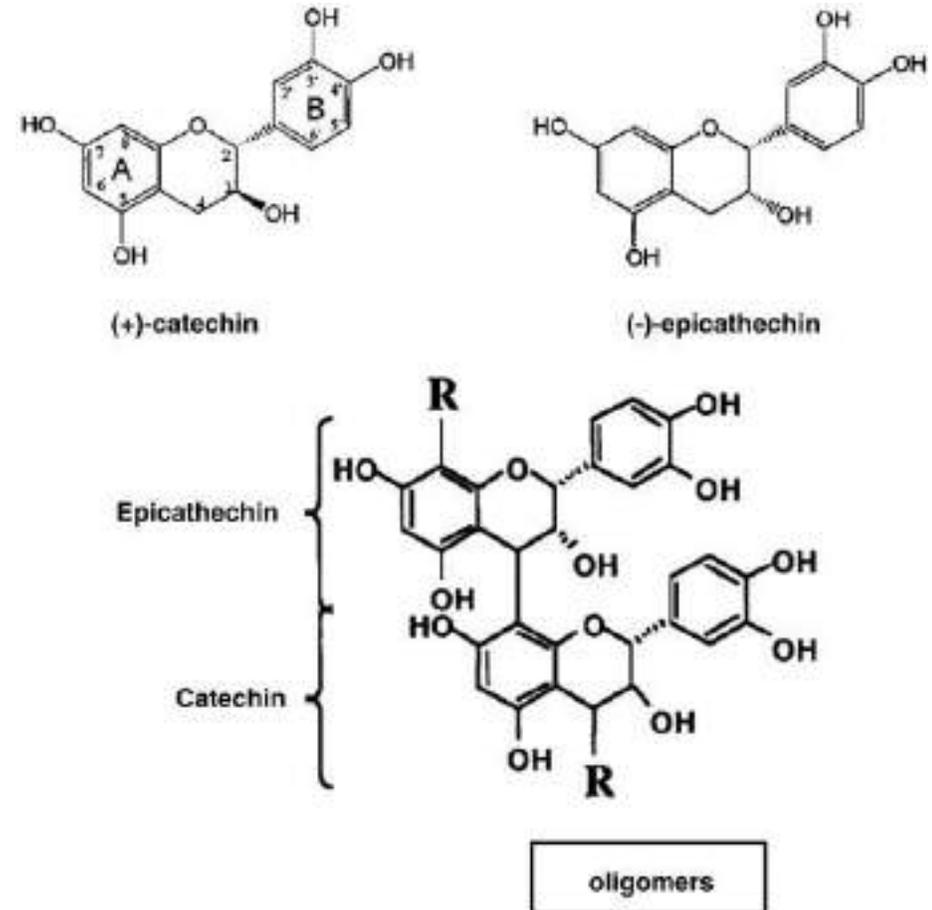
Taxifolin **a** 2.1

Ferulic acid **a** 0.5

Other including trimers, tetramers 19.0

From: <http://www.integratedhealth.com/infoabstract/pycdes.html>.

a Component which requires measurement of peak areas



Contents lists available at [ScienceDirect](#)

Fitoterapia

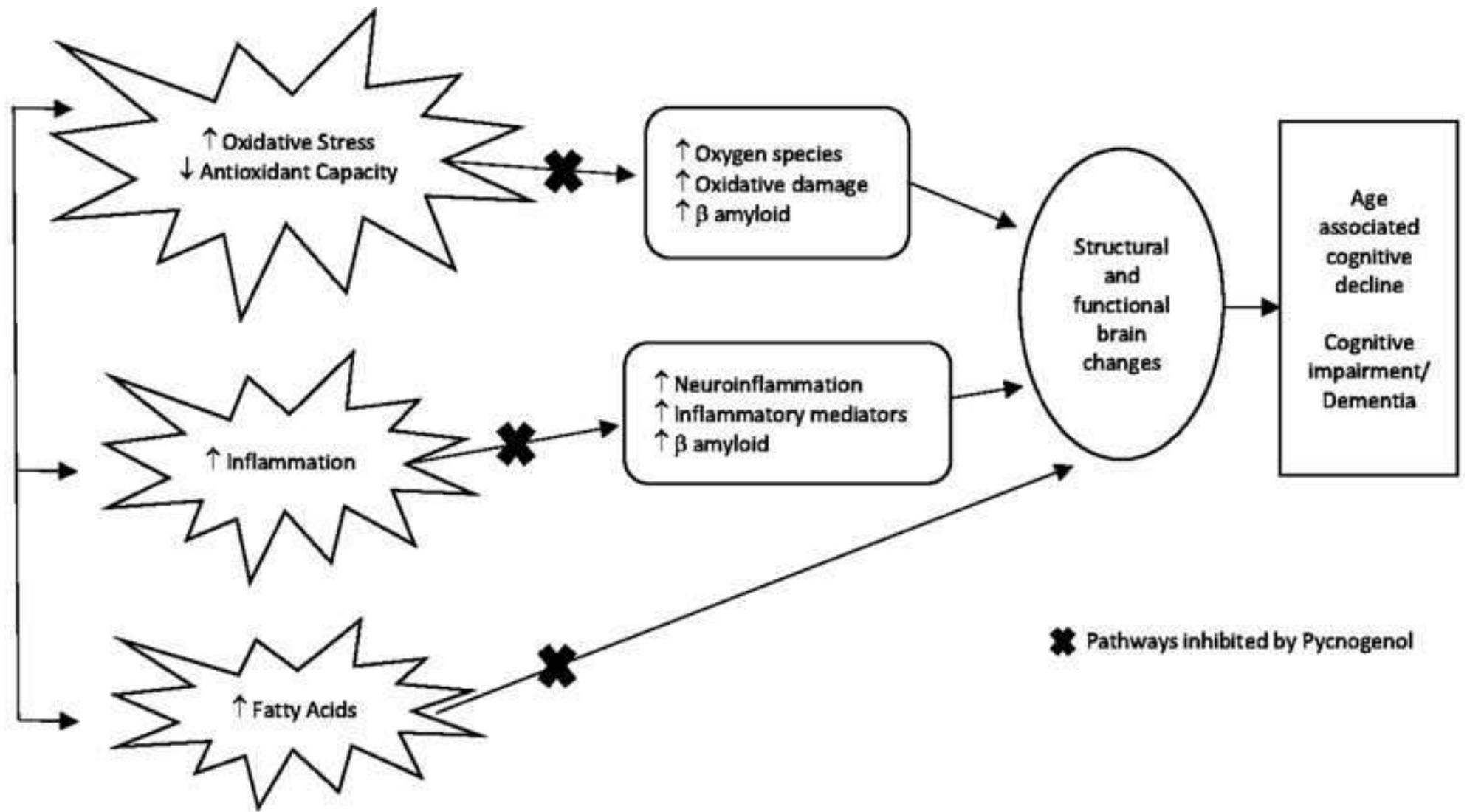
journal homepage: www.elsevier.com/locate/fitote

Review

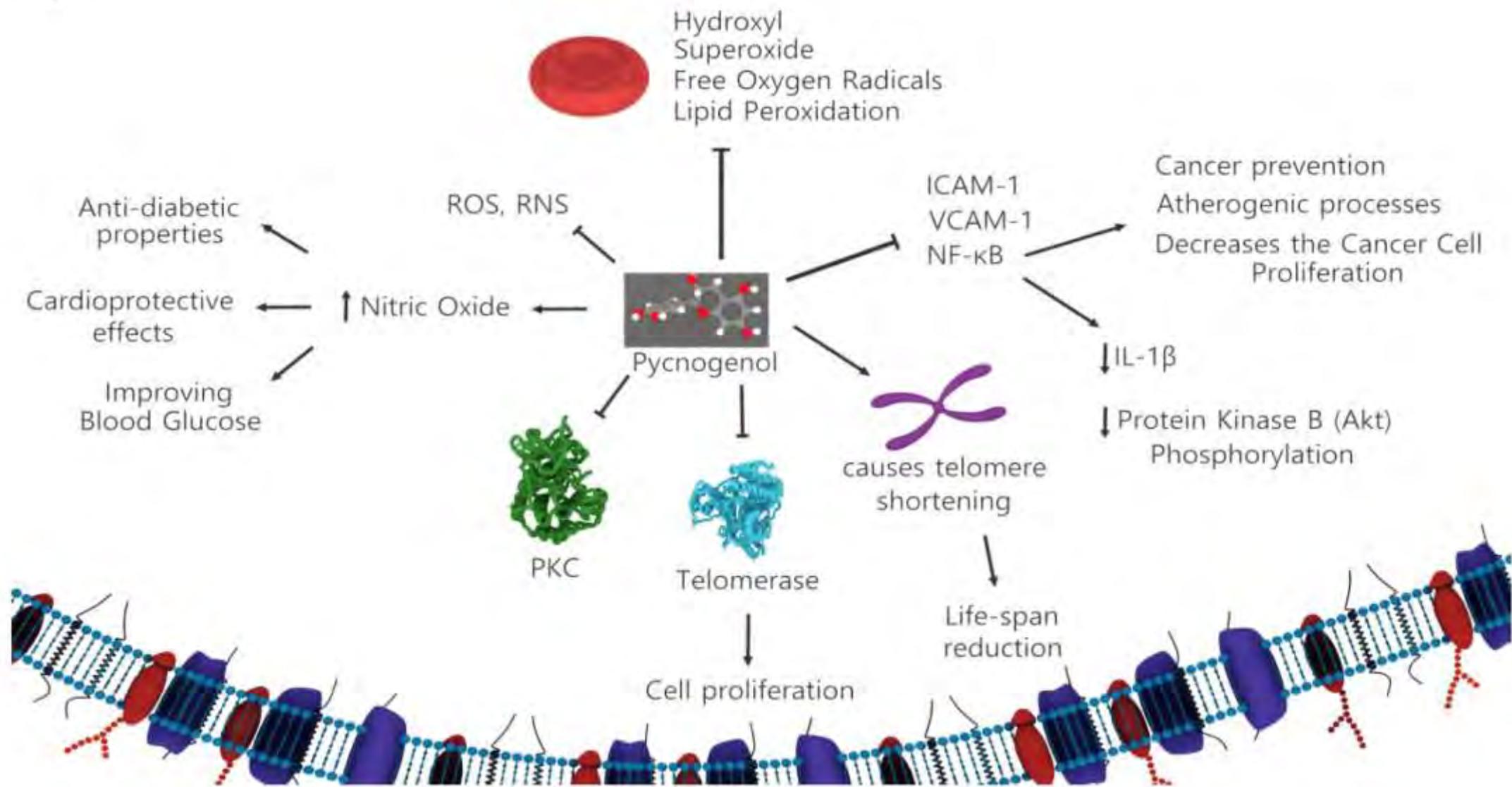
In 1535, a Jacques Cartier found his ship ice-bound in the St. Lawrence River, in Quebec. Having no fruits or vegetables, the crew began developing scurvy (symptoms of vitamin C deficiency). Native Americans told them to prepare a tea made of bark from a particular tree. In 1951, Jacques Masquelier reportedly read this account in Cartier's writings, and began searching for the active ingredients in the tea. By 1948, from peanut skin he had succeeded in isolating that substance named oligomeric proanthocyanidin (OPC), and had identified that it possessed vasoprotective (protective of blood vessels) potential

Property	Grape pip/seed extract	Pine bark extract
% Polyphenols	92%	84%
% Monomers (flavan-3-ol)	32%	38%
% Oligomers (proanthocyanidins)	68%	62%
Oligomer/monomer ratio	2.1	1.6
Polyphenol/monomer ratio	3.1	2.6
Polyphenol/oligomer ratio	1.5	1.6

From: Procyanidins de France – brochure available from Crossover Marketing 203-481-8863.



X Pathways inhibited by Pycnogenol



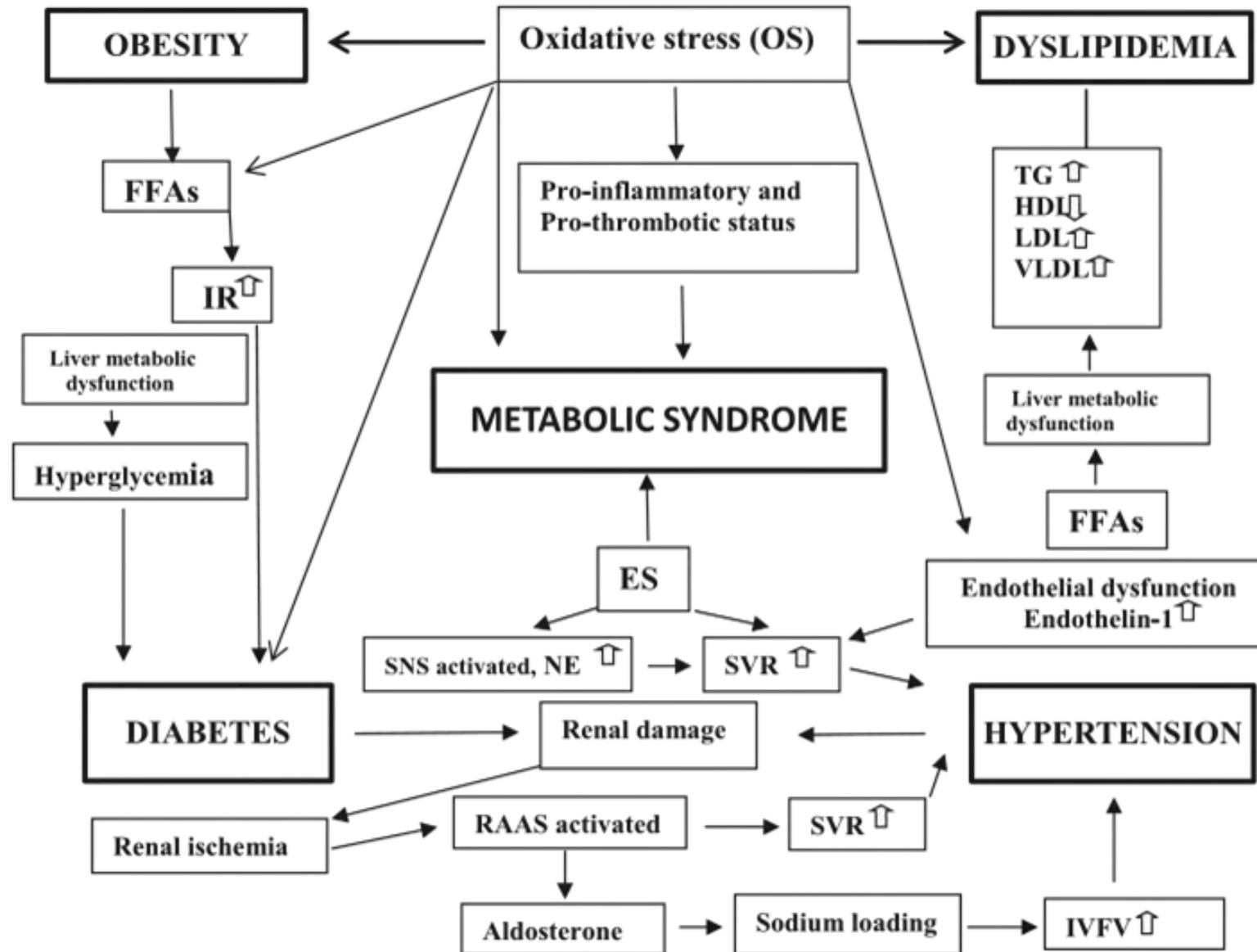
Supplementation with Pycnogenol® improves signs and symptoms of menopausal transition

[S Errichi¹](#), [A Bottari](#), [G Belcaro](#), [M R Cesarone](#), [M Hosoi](#), [U Cornelli](#), [M Dugall](#), [A Ledda](#), [B Feragalli](#)

Pycnogenol® was used by 38 women as daily supplement in a dosage of 100 mg over an eight week period and menopausal symptoms were evaluated by means of a scoring system, based on a total number of 33 common signs and symptoms. A parallel control group of 32 comparable women was also followed up for the same period. Pycnogenol® was well tolerated, no side effects were reported and the compliance was very good with 98.6% of tablets used as prescribed. A range of 33 menopausal symptoms were evaluated using a scoring system with values ranging from zero (absent) to maximum 4 (very serious).

Conclusion: Pycnogenol® significantly contributed to reduce signs and symptoms associated with menopausal transitions in women investigated in this study. Furthermore, Pycnogenol® improved the quality of life of most women and these benefits may be at least in part attributed to decreased oxidative stress levels.

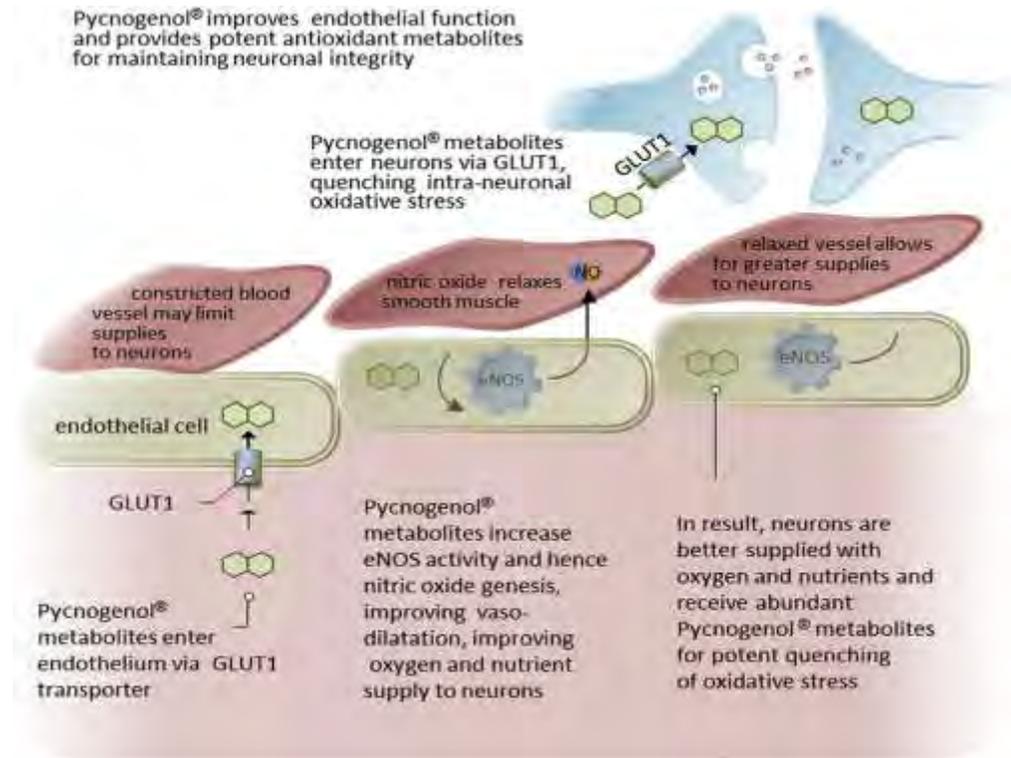
Pycnogenol® in Metabolic Syndrome and Related Disorders



S. N°	Disease condition	Target organ/parameter(s)		Beneficial effect	Reference
1	Metabolic syndrome	Blood pressure, total cholesterol, fasting glucose CRP levels ^a	↓	Beneficial effects in hypertension dyslipidaemia and diabetes. Kidney function improved.	(Cesarone et al., 2008b) (Stuard et al., 2010)
2	Metabolic syndrome	Blood pressure ^a , HbA _{1c} ^a	↓	Beneficial effects in hypertension and diabetes.	(Stuard et al., 2010)
3	Metabolic syndrome	Blood pressure ^a , fasting blood glucose ^a triglycerides ^a plasma free radicals ^a waist circumference ^a HDL	↓	Beneficial effects on BP, TGs, obesity and anti-oxidant effects are evident.	(Belcaro et al., 2013)
4	Diabetes mellitus	Fasting blood glucose ^a postprandial glucose ^a endothelin-I ^a	↓	Dose-dependent effects	(Liu et al., 2004b, Liu et al., 2004a)
5	Diabetes mellitus	Fasting blood glucose ^a postprandial glucose ^a endothelin-I Prostacyclin ^a nitric oxide (NO) ^a	↓	Beneficial effects in diabetes, endothelial function improved. Produces potent inhibition (IC ₅₀ about 5 µg/mL) of α-glucosidase	(Liu et al., 2004b, Liu et al., 2004a) (Schafer and Hogger, 2007)
6	Diabetes and Hypertension	Fasting blood glucose ^{**} HbA _{1c} ^a blood pressure urinary albumin	↓	Beneficial effects in diabetes and hypertension. Renal and endothelial functions improved.	(Zibadi et al., 2008)
7	Hypertension	Systolic BP ^a diastolic BP serum thromboxane ^a	↓	Decrease in vasoconstrictor component.	(Hosseini et al., 2001)
8	Hypertension	Endothelin-I ^a Prostacyclin ^a	↓	Endothelial function improved.	(Liu et al., 2004a)
9	Hypertension	Edema induced by antihypertensive drugs ^{ba}	↓	Improved peripheral microcirculation.	(Belcaro et al., 2006)
10	Hypertension	Diastolic BP ^a urinary albumin ^a serum creatinine ^a CRP ^a	↓	Renal function improved	(Cesarone et al., 2010)

The multifactorial contributions of Pycnogenol for cognitive function improvement

The ability of Pycnogenol metabolites to reach into neuronal cells via the GLUT1 transporter where they extinguish oxidative stress in neurons, explains the cognition improvements witnessed in clinical trials carried out to date



Il presente opuscolo contiene informazioni scientifiche destinate agli Operatori del settore e non può essere divulgato ai Consumatori finali. Gli integratori alimentari non vanno intesi come sostituti di una dieta variata ed equilibrata e di uno stile di vita sano. Gli integratori inoltre non sostituiscono le prescrizioni mediche. In nessuna parte di questa lezione si vuole suggerire una prescrizione medica e quindi non si accettano responsabilità mediche e legali relative all'uso incongruo delle informazioni scientifiche fornite.