STRAWBERRY AND HEALTH: AN EXTRAORDINARY LINKAGE

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Bordeaux, 27th March 2014

BERRIES: AN INNOVATIVE HEALTHY CHOICE

Relevant biological and nutritional qualities

STRAWBERRY (Fragaria X Ananassa, Duch.)

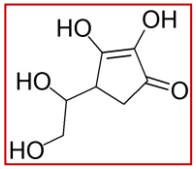
✓One of the most commonly consumed berries, both in fresh and processed forms;

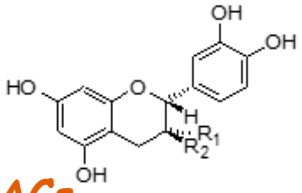
✓Relevant source of bioactive compounds due to its high level of Vitamin C, folate and phenolic constituents which express relevant antioxidant capacities;

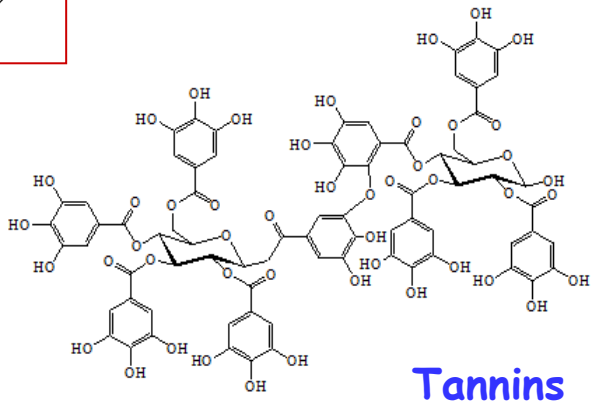
✓The most studied berry from the agronomic, genomic and nutritional point of view

STRAWBERRY (Fragaria x ananassa, Duch.)

Vitamin C

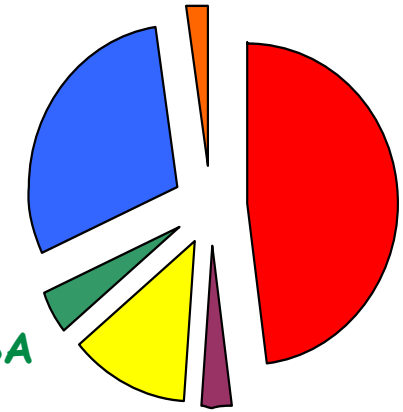


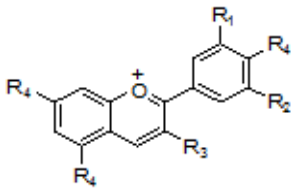




Flavanols/PACs

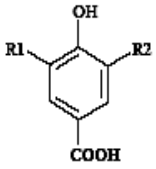
Anthocyanins





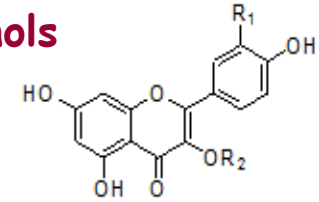
Tannins

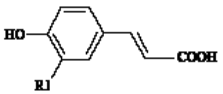
HBA

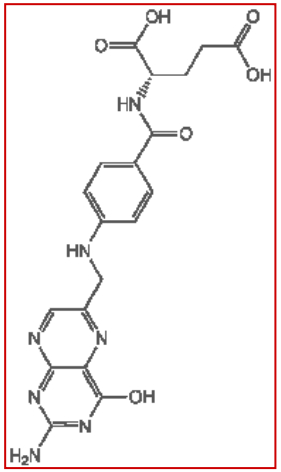


HCA

Flavonols

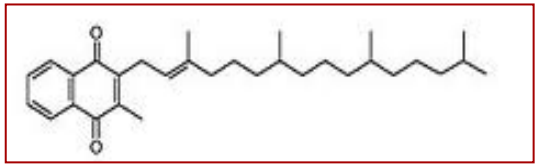






Folate

Vitamin E



STRAWBERRY QUALITY

JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

Antioxidants, Phenolic Compounds, and Nutritional Quality of Different Strawberry Genotypes

Sara Tulipani, Bruno Mezzetti, Franco Capocasa, Stefano Bompadre, Jules Beekwilder, C. H. Ric de Vos, Esra Capanoglu, Arnaud Bovy, and Maurizio Battino

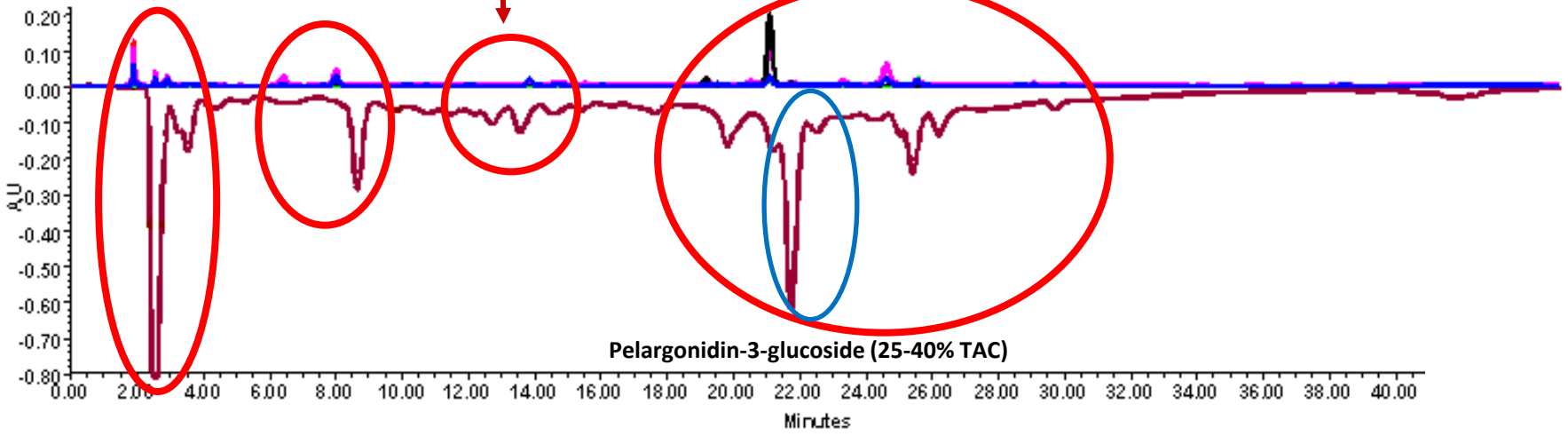
J. Agric. Food Chem., 2008, 56 (3), 696-704 • DOI: 10.1021/jf0719959 • Publication Date (Web): 23 January 2008

Highly-polar antioxidants
+++ vitamin C (>30% TAC)

Phenolic acids

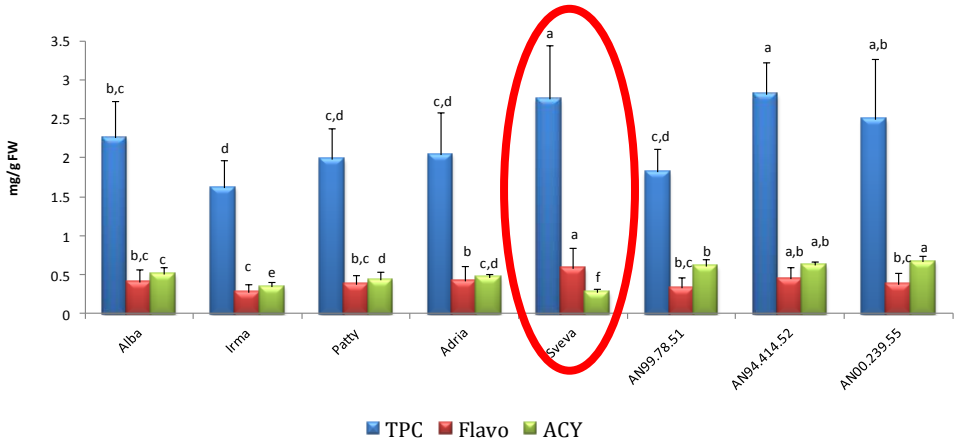
HCA Derivatives

+++ Anthocyanins/EA deriv.
-- Flavonols



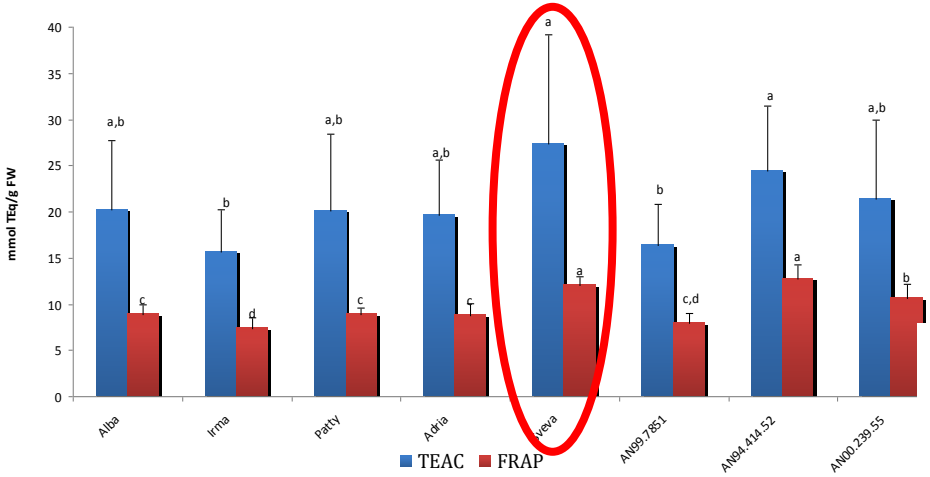
Pelargonidin-3-glucoside (25-40% TAC)

STRAWBERRY QUALITY



Total content of phenols, flavonoids and anthocyanins

Total Antioxidant capacity



IN VITRO studies

Human dermal fibroblast - HDF

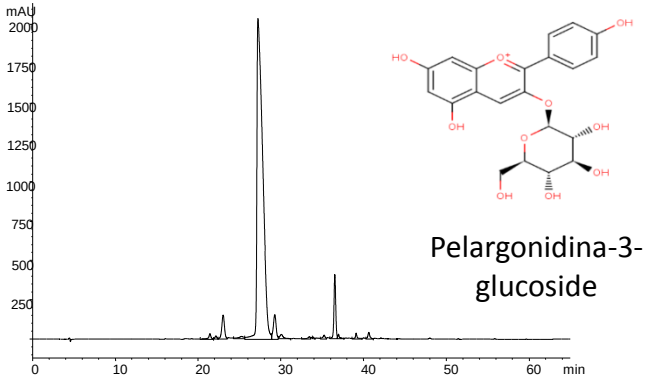
JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY
Article
pubs.acs.org/JAFC

Photoprotective Potential of Strawberry (*Fragaria* × *ananassa*) Extract against UV-A Irradiation Damage on Human Fibroblasts

Francesca Giampieri,[†] Josè M. Alvarez-Suarez,[†] Sara Tulipani,[‡] Ana M. Gonzàles-Paramàs,[§] Celestino Santos-Buelga,[§] Stefano Bompadre,[∥] José L. Quiles,[⊥] Bruno Mezzetti,[#] and Maurizio Battino*[,†]

dx.doi.org/10.1021/jf2050665x | J. Agric. Food Chem. 2012, 60, 2322–2327

HPLC-DAD-MS analysis



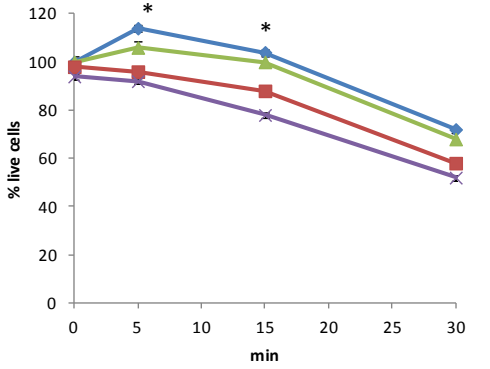
Pelargonidina-3-glucoside

- High content of pelargonidin-3-glucoside
- Relevant total antioxidant capacity
- High content of Vitamin C

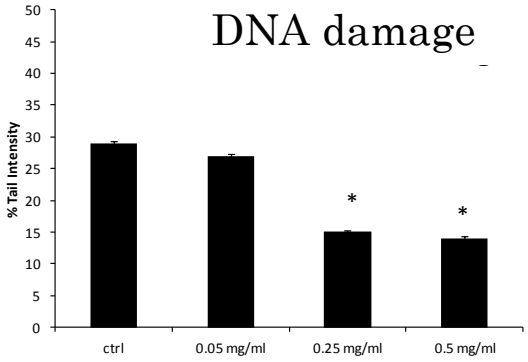
Incubation for 24 hours with different concentrations of the extracts (0.5 – 0.25 – 0.05 mg/ml)

UV-A treatment 275 kJ/m²

Cell viability



DNA damage



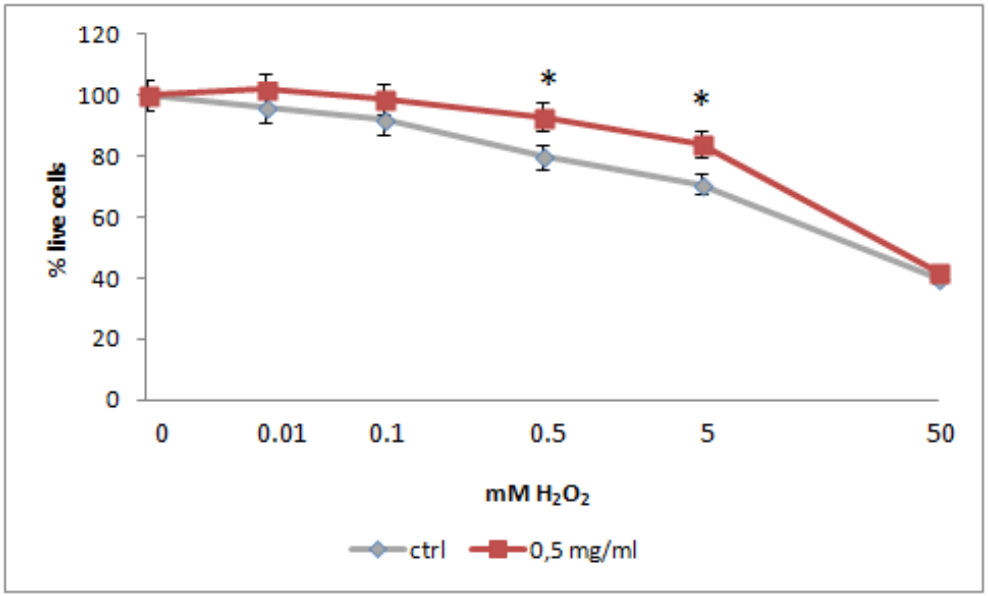
IN VITRO studies

Human dermal fibroblast - HDF

Incubation for 24 hours with different concentrations of the extracts (0.5 – 0.25 – 0.05 mg/ml)

H_2O_2 treatment / 1h

Cells Viability

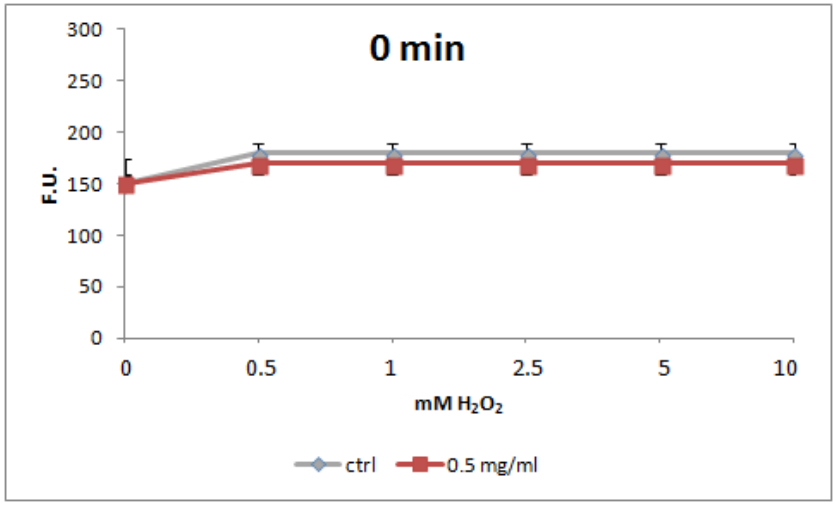


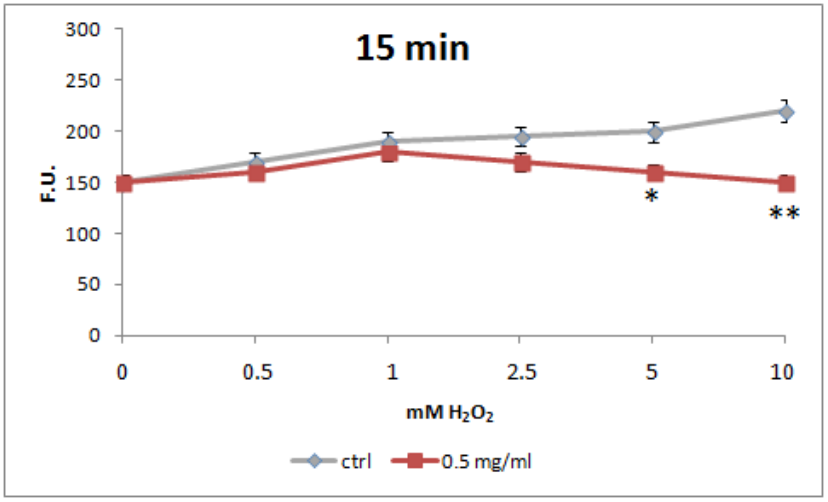
IN VITRO studies

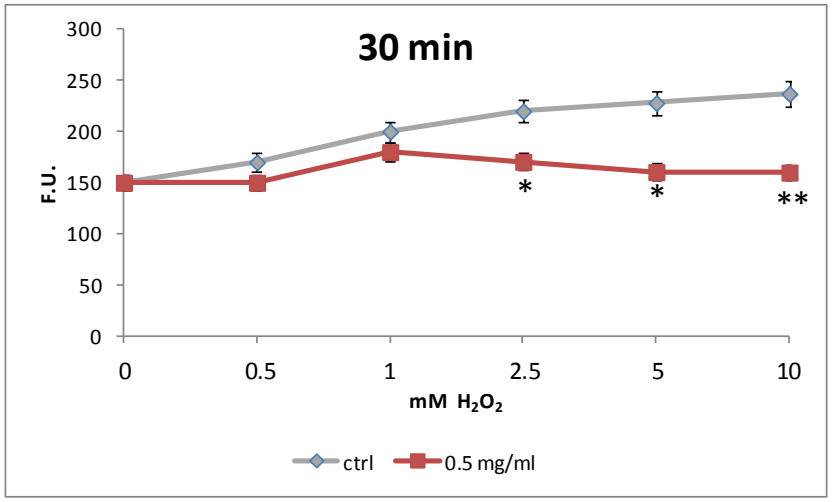
H_2O_2 treatment / 1h

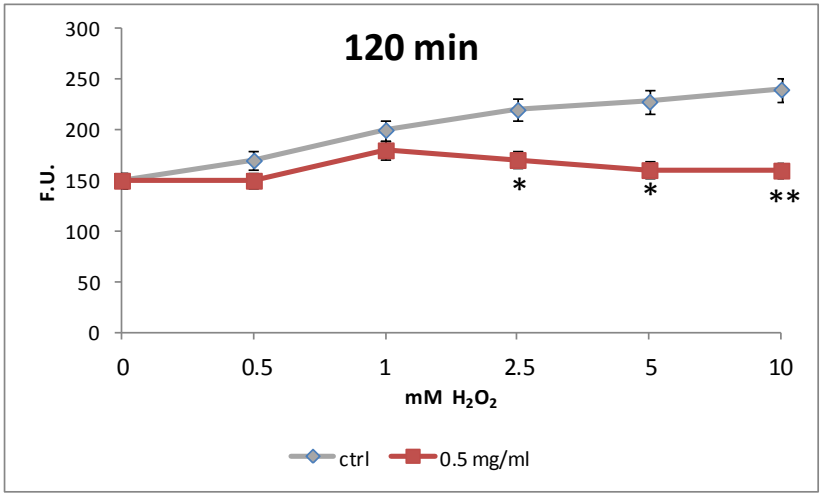
Human dermal fibroblast - HDF

Intracellular ROS





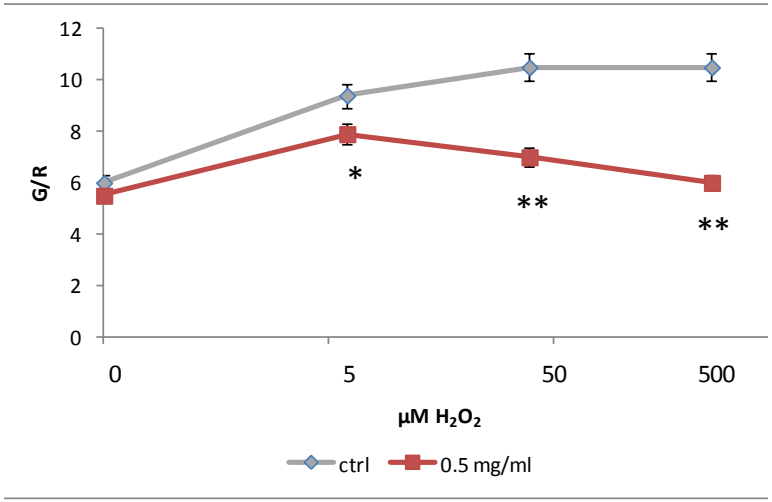




IN VITRO studies

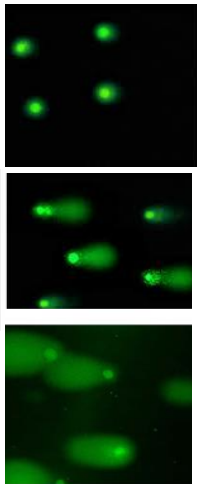
H_2O_2 treatment / 1h

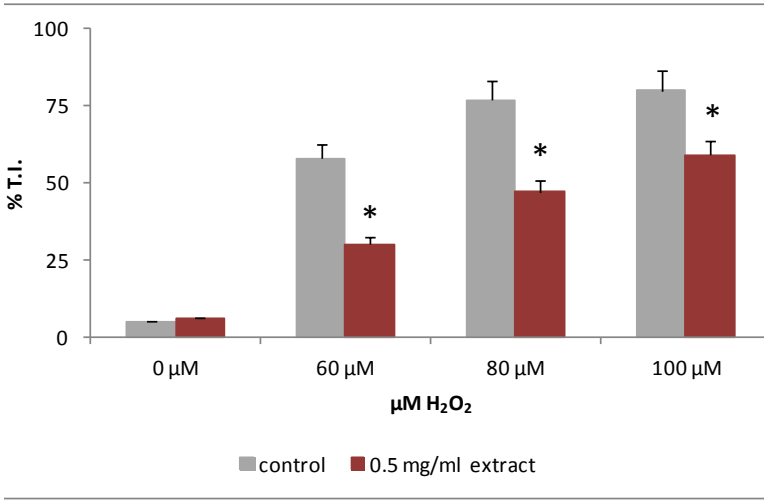
Human dermal fibroblast - HDF



Lipid peroxidation

DNA damage

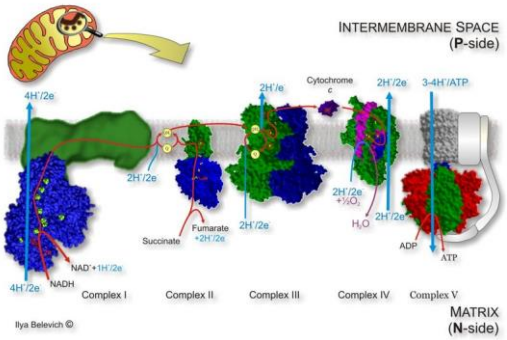




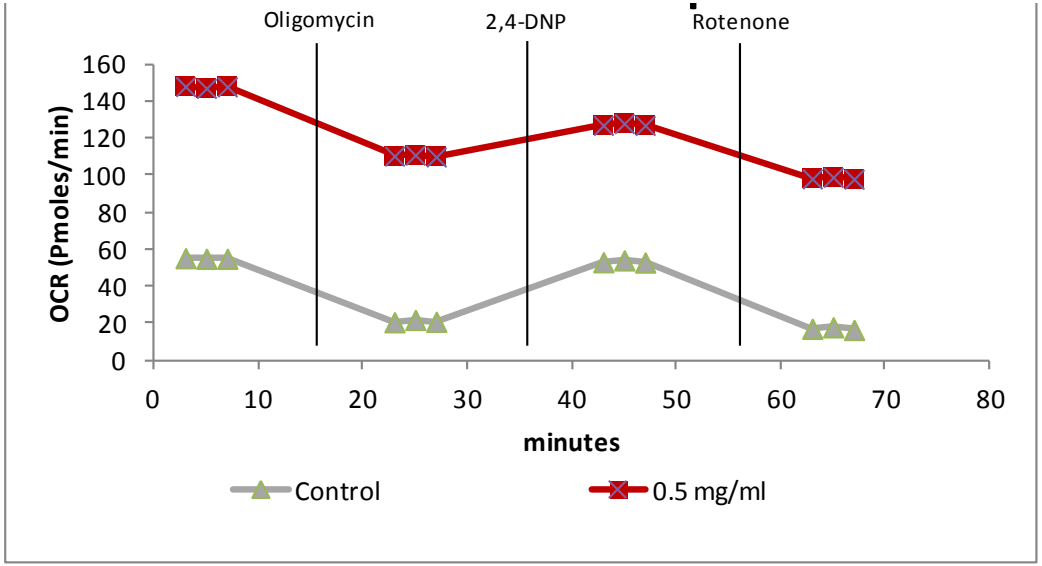
IN VITRO studies

H_2O_2 treatment / 1h

Human dermal fibroblast - HDF



Seahorse XF-24: Mitochondrial respiration (OCR)

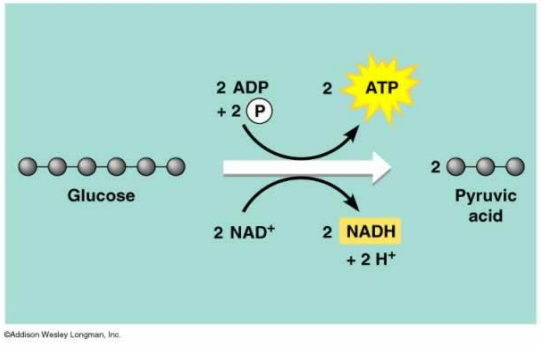


20.000 HuDe; stress agent H_2O_2 5 mM; strawberry methanolic extract applied 0.5 mg/ml; inhibitors concentration: Oligomycin 1 µg/ml, 2,4-Dinitrophenol (2-DNP) 100 µM, Rotenone 1µM

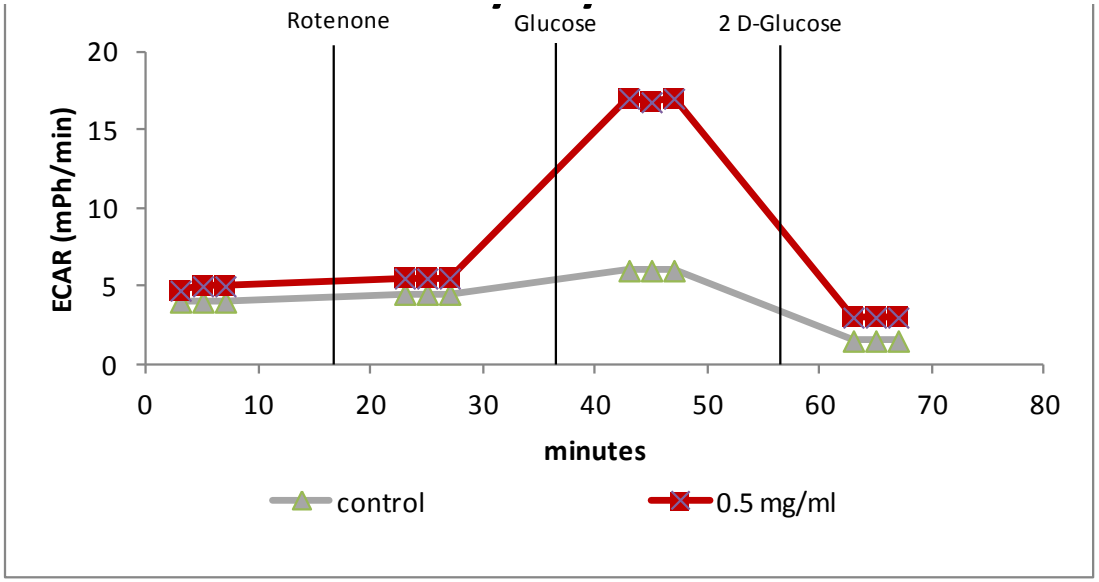
IN VITRO studies

H_2O_2 treatment / 1h

Human dermal fibroblast - HDF



Seahorse XF-24: Glycolysis (ECAR)



20.000 HuDe; stress agent H_2O_2 5 mM; strawberry methanolic extract applied 0.5 mg/ml; inhibitor concentrations:

Rotenone 3 µg/ml, Glucose 10 mM, 2-DeoxyGlucose (2-DG) 100mM

IN VITRO studies

Human dermal fibroblast - HDF

Incubation for 24 hours with different concentrations of the extracts (0.5 – 0.25 – 0.05 mg/ml)

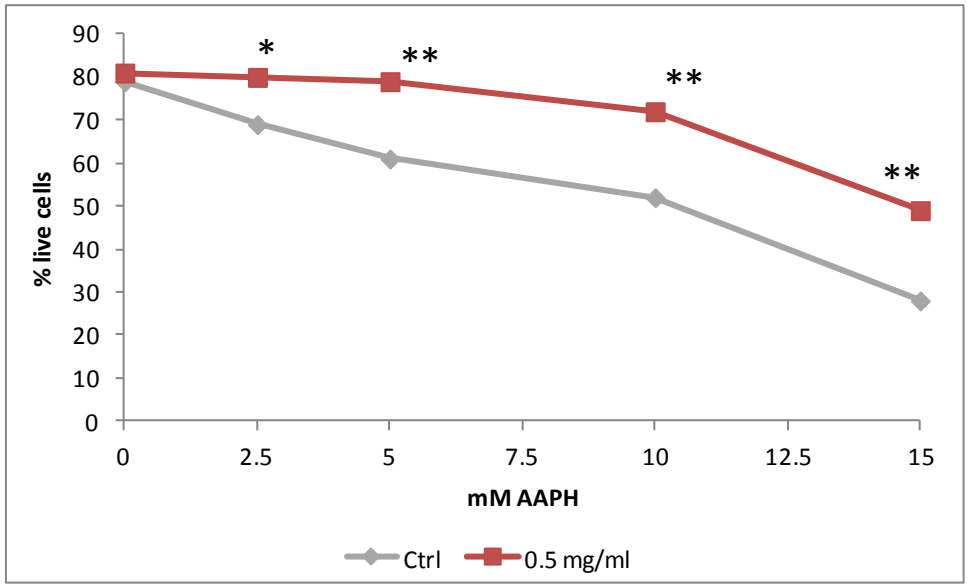
AAPH treatment / 1h

Submitted

Anthocyanin-rich strawberry extract protects against oxidative stress damage and improves mitochondrial functionality in human dermal fibroblasts exposed to oxidant agent.

Francesca Giampieri, José M. Alvarez-Suarez, Luca Mazzoni , Tamara Y. Forbes-Hernandez, Massimiliano Gasparrini, Ana M. Gonzàlez-Paramàs, Celestino Santos-Buelga, Josè L. Quiles, Bruno Mezzetti, and Maurizio Battino

Cells Viability



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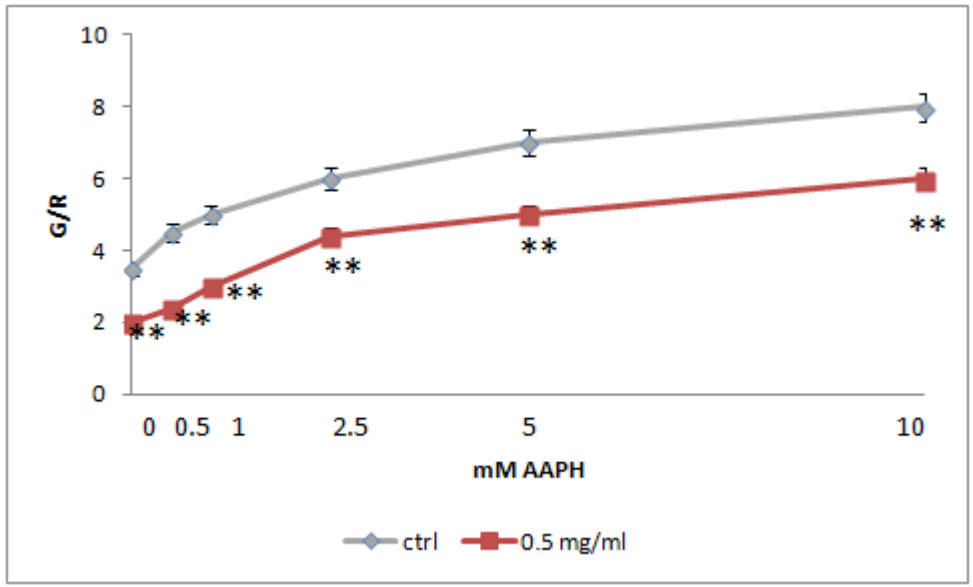
Lipid peroxidation



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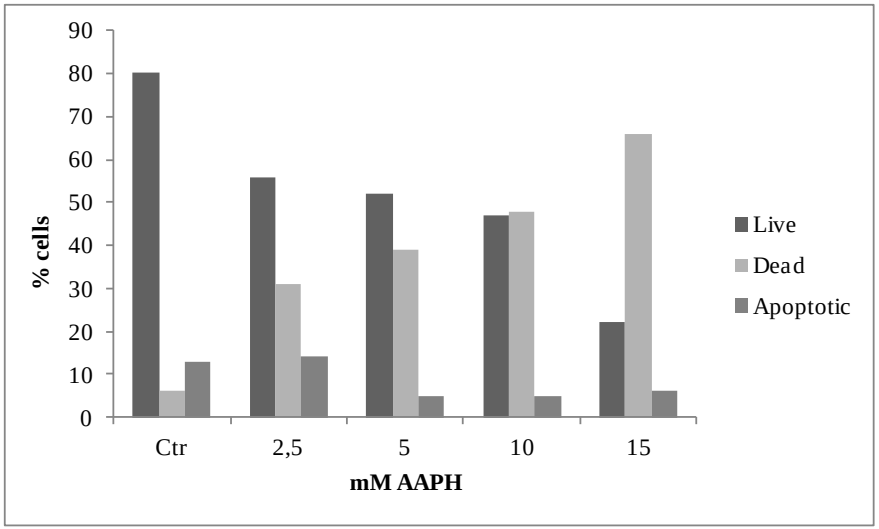
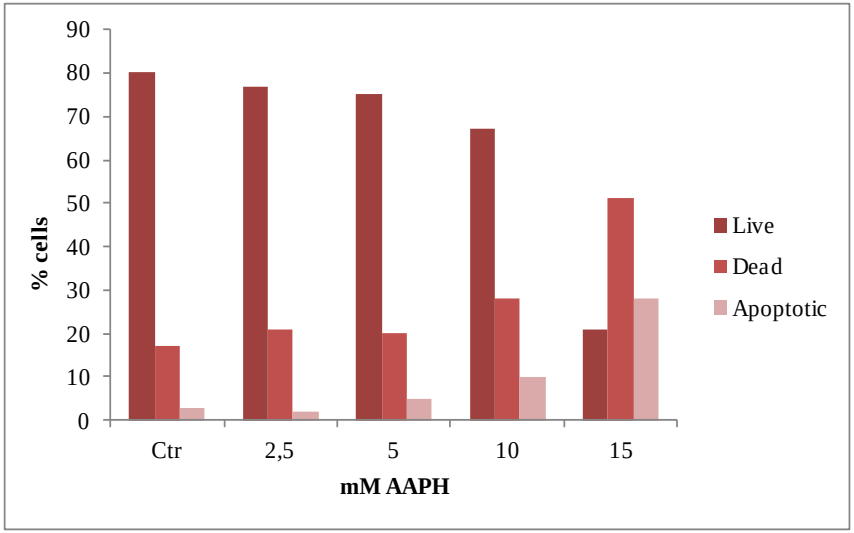
Live/dead/apoptosis cells by

TALI

Without strawberry



With strawberry



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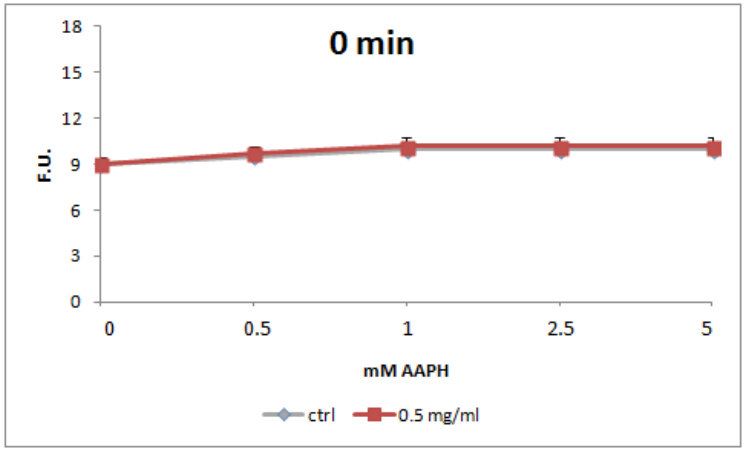
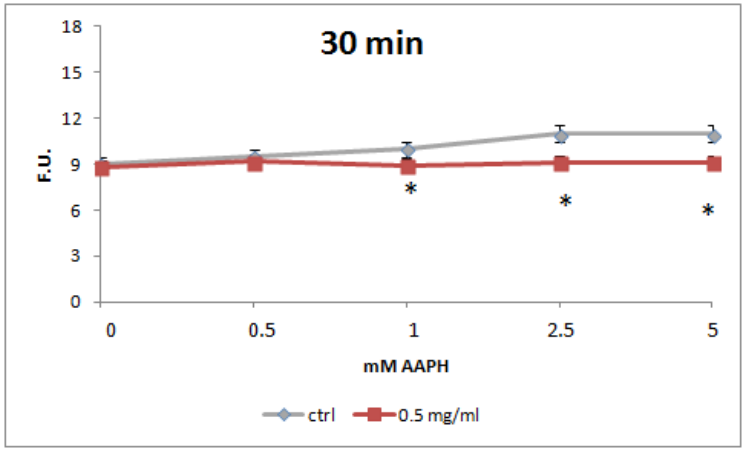
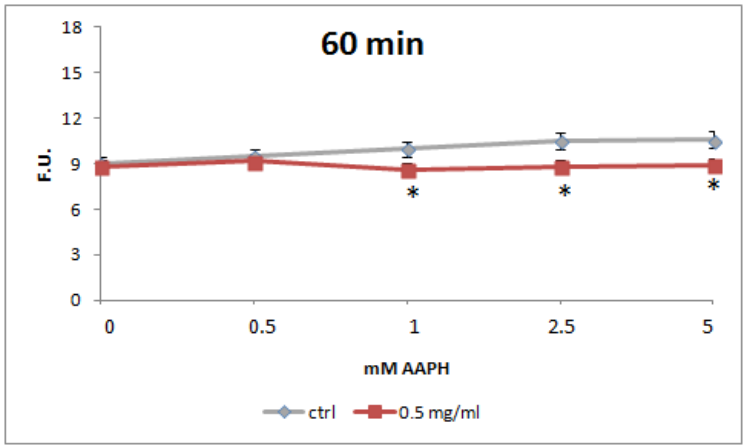
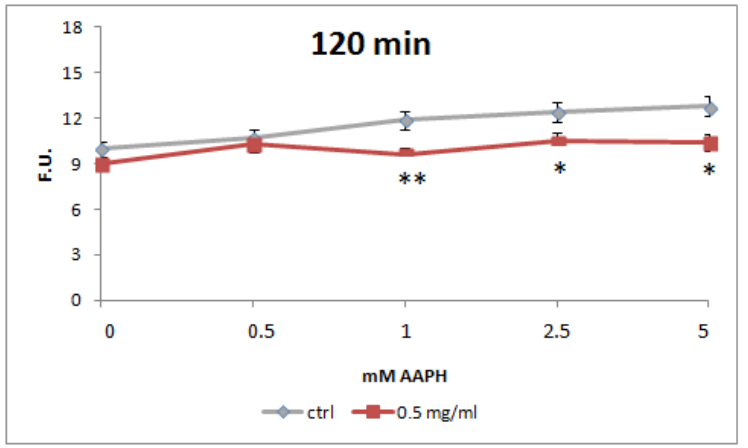
Intracellular ROS









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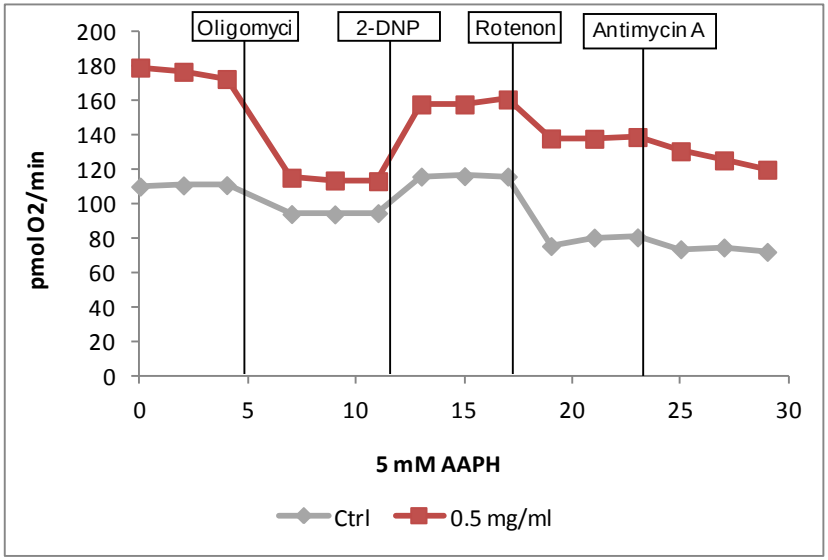
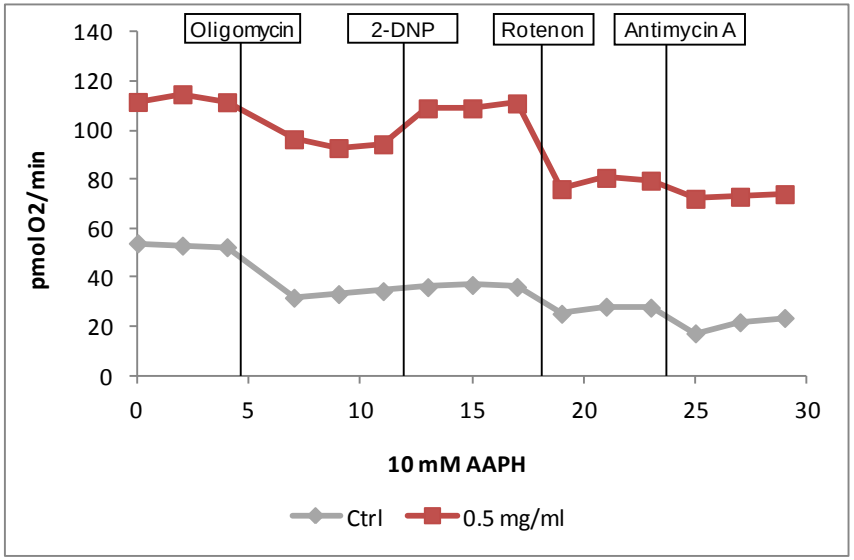
Mithocondrial respiration





20.000 HuDe; stress agent AAPH; strawberry methanolic extract applied 0.5 mg/ml; inhibitors concentration: Oligomycin 1 µg/ml, 2,4-Dinitrophenol (2-DNP) 100 µM, Rotenone 1µM, Antimycin A 1µM

IN VITRO VERSUS IN VIVO EVIDENCE: HOW TO BYPASS THE GAP?

In vitro effects

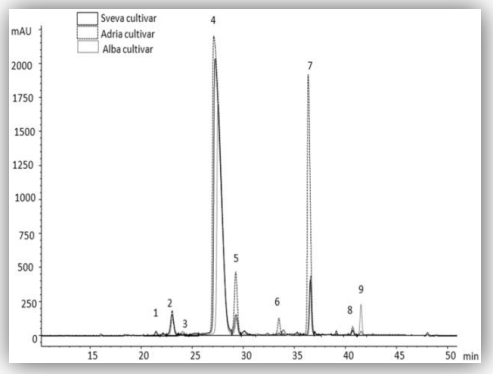
In vivo effects

Few literature data on strawberry intake and antioxidant status

ON ANIMALS studies

Strawberry polyphenolic extract

HPLC-DAD-MS analysis



OPEN ACCESS Freely available online
PLoS one

Strawberry Polyphenols Attenuate Ethanol-Induced Gastric Lesions in Rats by Activation of Antioxidant Enzymes and Attenuation of MDA Increase

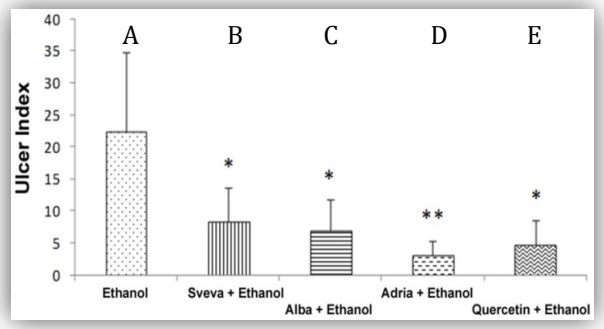
José M. Alvarez-Suarez[1], Dragana Dekanski[2], Slavica Ristić[2], Nevena V. Radonjić[3], Nataša D. Petronijević[3], Francesca Giampieri[1], Paola Astolfi[4], Ana M. González-Paramás[5], Celestino Santos-Buelga[5], Sara Tulipani[6], José L. Quiles[7], Bruno Mezzetti[8], Maurizio Battino[1]*

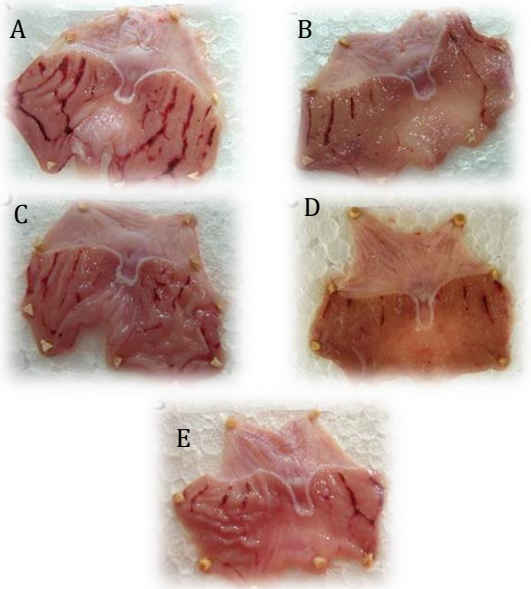
October 2011 | Volume 6 | Issue 10 | e25878

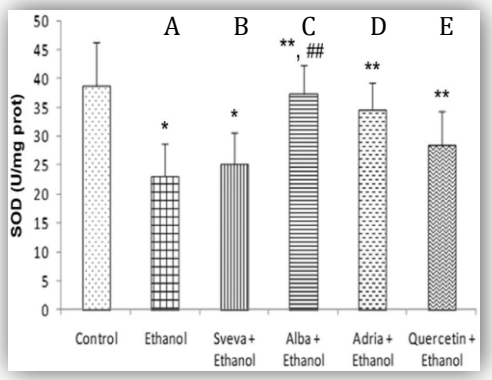
ETHANOL
- Widespread gastric lesion
- Oxidative Stress

The rats daily received 40 mg/kg body weight of strawberry crude extract intragastrically using a gavage for 10 days

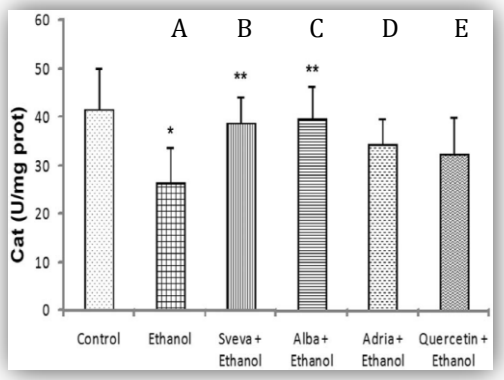
ULCER INDEX







SOD ACTIVITY



CAT ACTIVITY

ON ANIMALS studies

JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY
Article
pubs.acs.org/JAFC

Doxorubicin-Induced Oxidative Stress in Rats Is Efficiently Counteracted by Dietary Anthocyanin Differently Enriched Strawberry (*Fragaria* × *ananassa* Duch.)

Jacopo Diamanti,[†] Bruno Mezzetti,[†] Francesca Giampieri,[†] José M. Alvarez-Suarez,[‡] José L. Quiles,[§] Adrian Gonzalez-Alonso,[§] Maria del Carmen Ramirez-Tortosa,[⊗] Sergio Granados-Principal,[⊗] Ana M. Gonzáles-Paramás,[⊥] Celestino Santos-Buelga,[⊥] and Maurizio Battino*[‡]

SVEVA ↓ **ACY** ↑ **TAC**

ADRIA ↑ **ACY** ↓ **TAC**

Peak	Tentative identification	Adria cultivar (mg/kg)	Sveva cultivar (mg/kg)
1	(Epi)afzelechin-(4→8)Pg-3-glucoside	3.798 ± 0.4	1.754 ± 0.1
2	Cy-3-glucoside	32.232 ± 2.1	25.974 ± 2.2
3	Pg 3,5-diglucoside	0.588 ± 0.0	0 ± 0.0
4	Pg 3-glucoside	1157.376 ± 12.0	790.234 ± 7.0
5	Pg 3-rutinoside	97.848 ± 4.0	26.176 ± 2.0
6	Pg 3-malonylglucoside	32.562 ± 3.0	45.62 ± 2.2
7	Pg 3-acetylglucoside	7.114 ± 4.0	3.284 ± 1.0
	Total Anthocyanin Content	1331.518 ± 4.6	893.042 ± 2.3

ON ANIMALS studies

JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY
Article
pubs.acs.org/JAFC

Doxorubicin-Induced Oxidative Stress in Rats Is Efficiently Counteracted by Dietary Anthocyanin Differently Enriched Strawberry (*Fragaria* × *ananassa* Duch.)

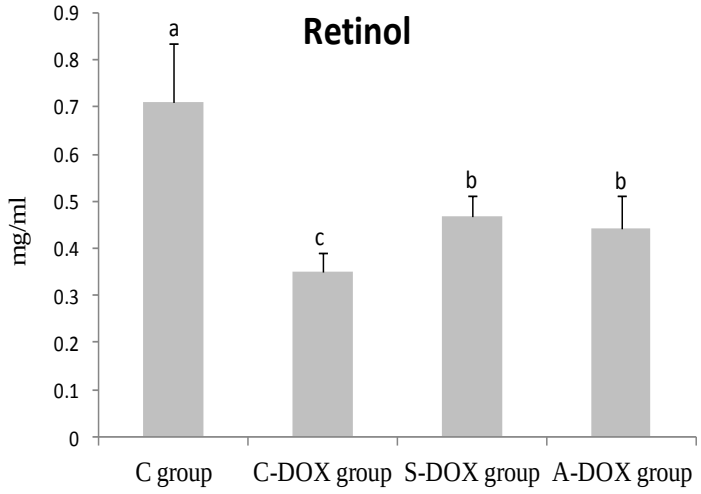
Jacopo Diamanti,[†] Bruno Mezzetti,[†] Francesca Giampieri,[†] José M. Alvarez-Suarez,[‡] José L. Quiles,[§] Adrian Gonzalez-Alonso,[§] Maria del Carmen Ramirez-Tortosa,[⊗] Sergio Granados-Principal,[⊗] Ana M. Gonzáles-Paramás,[⊥] Celestino Santos-Buelga,[⊥] and Maurizio Battino*[‡]

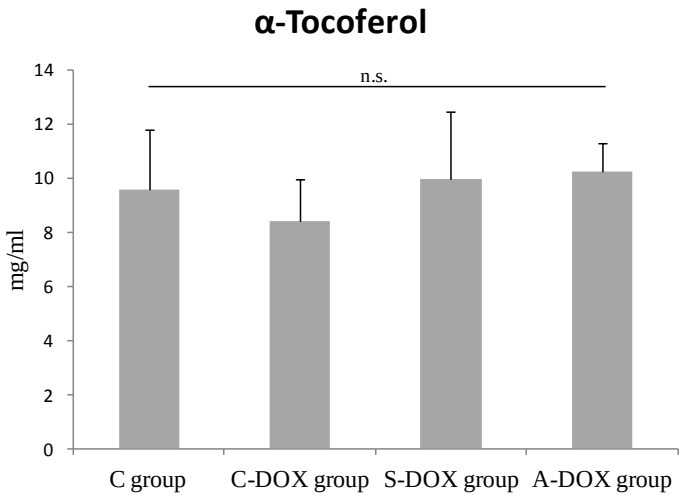
16 weeks supplementation

Diet with 10% strawberry

Doxorubicin injection

SVEVA	Plasma	ADRIA
↑ = retinol content		retinol content = ↑
α tocopherol level		α tocopherol level





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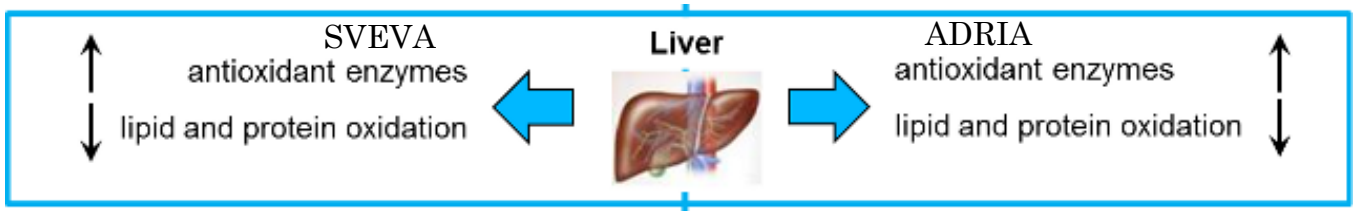

	GSH[a]	Protein carbonyl content[a]	TBARS[a]	Hydroperoxides[a]
C group	164.39 ± 2.54[a]	7.65 ± 0.23[b]	0.46 ± 0.16[b]	11.42 ± 0.04[c]
C-DOX group	96.13 ± 1.27[c]	24.33 ± 2.54[a]	0.90 ± 0.15[a]	20.4 ± 0.28[a]
A-DOX group	139.85 ± 1.04[b]	8.74 ± 0.93[b]	0.37 ± 0.06[b]	12.22 ± 0.37[bc]
S-DOX group	132.67 ± 0.34[b]	5.71 ± 1.15[b]	0.42 ± 0.01[b]	12.96 ± 0.05[b]

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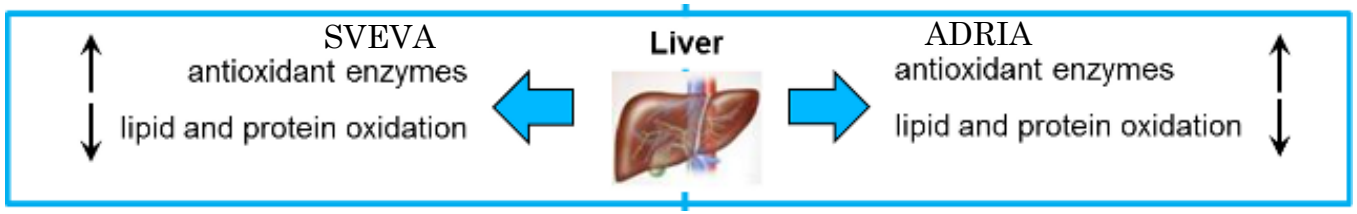

	GST[a]	GPx[a]	GR[a]	SOD[b]	Catalase[b]
C group	430.01 ± 3.95[a]	0.55 ± 0.04[a]	170.96 ± 5.75[a]	123.33 ± 1.81[a]	18.98 ± 1.52[a]
C-DOX group	221.42 ± 27.49[b]	0.31 ± 0.03[b]	83.81 ± 4.61[b]	45.66 ± 0.05[c]	9.73 ± 0.78[b]
A-DOX group	425.26 ± 33.43[a]	0.53 ± 0.07[a]	167.73 ± 6.02[a]	106.75 ± 2.68[ab]	19.90 ± 1.78[a]
S-DOX group	424.02 ± 4.37[a]	0.52 ± 0.03[a]	164.13 ± 3.41[a]	89.18 ± 2.54[b]	19.40 ± 1.01[a]

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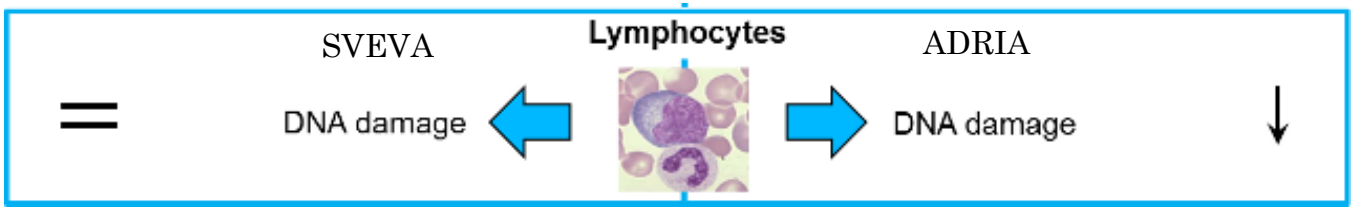

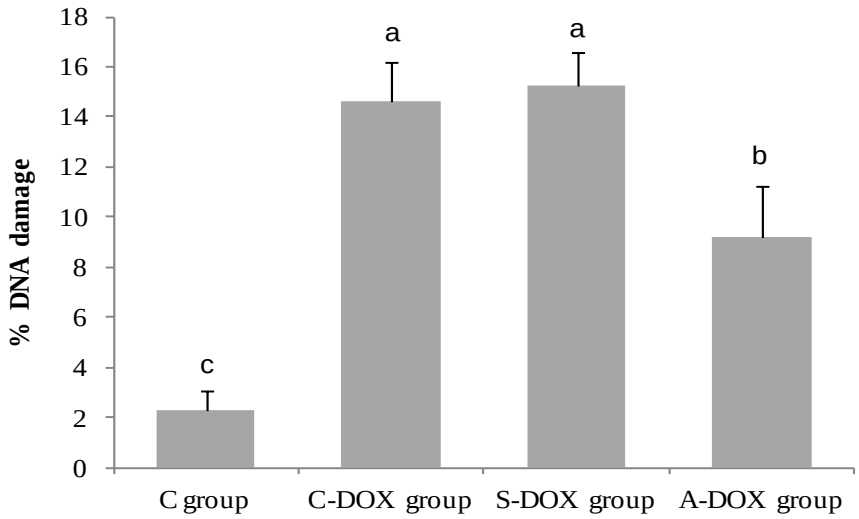

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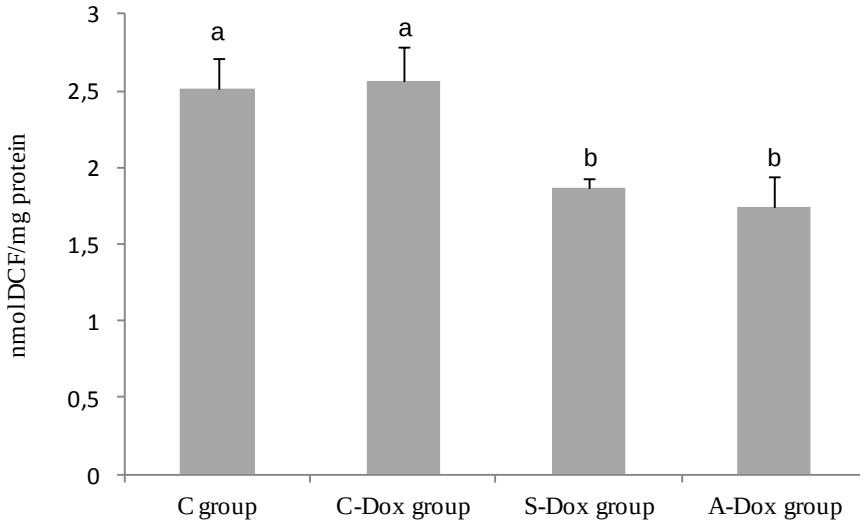
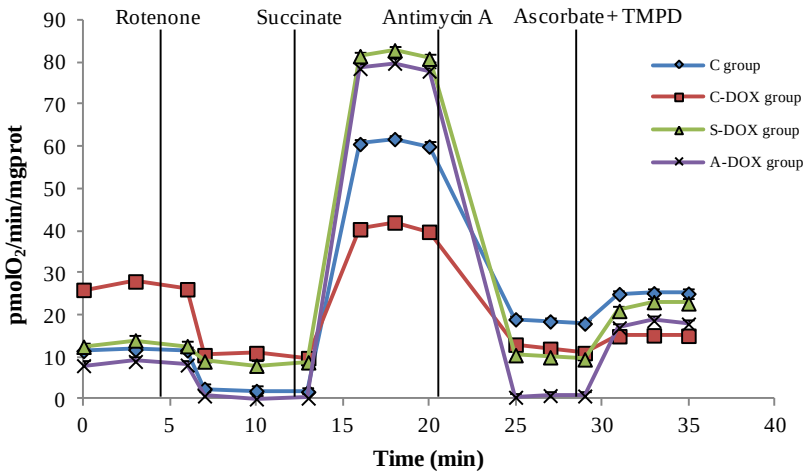
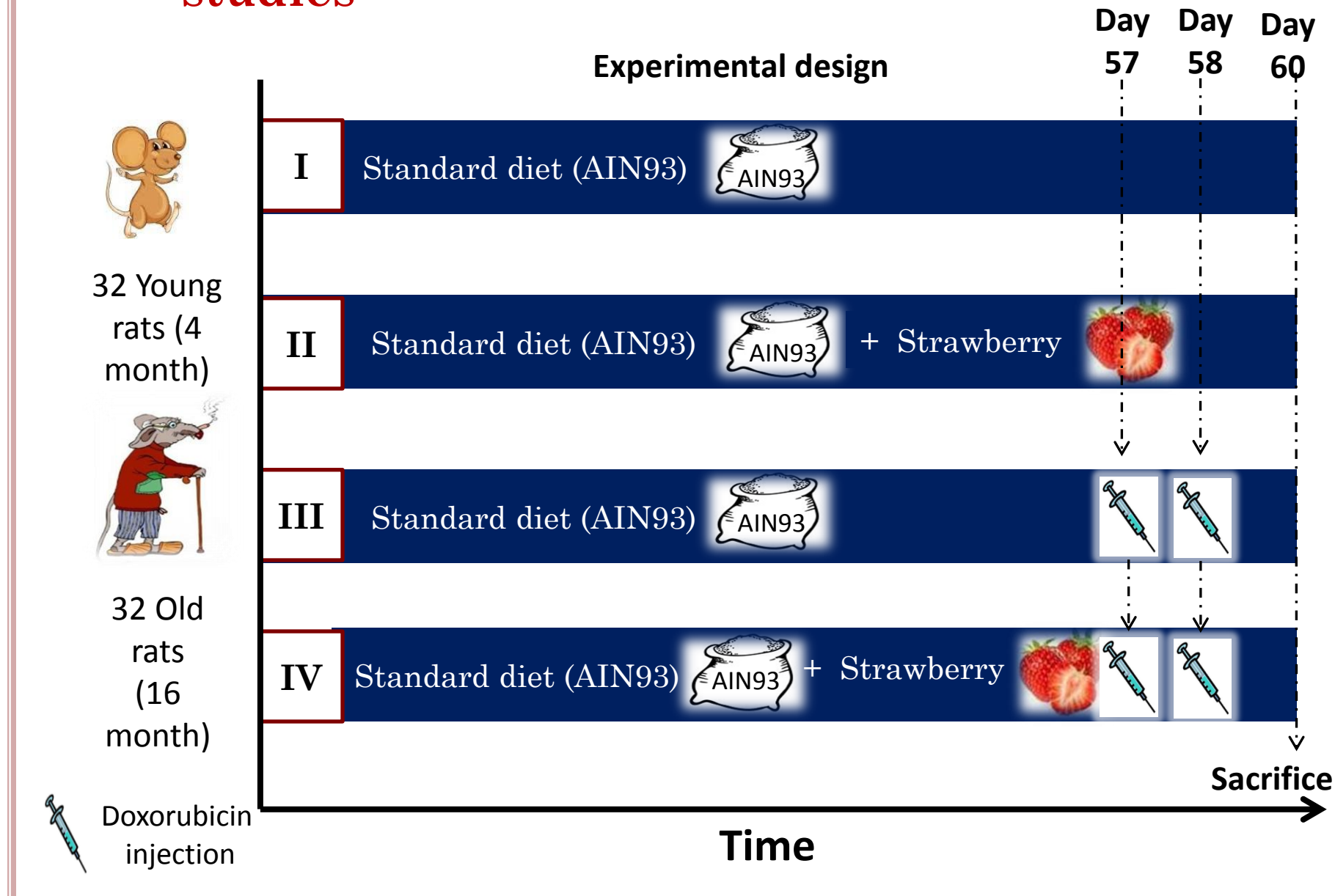




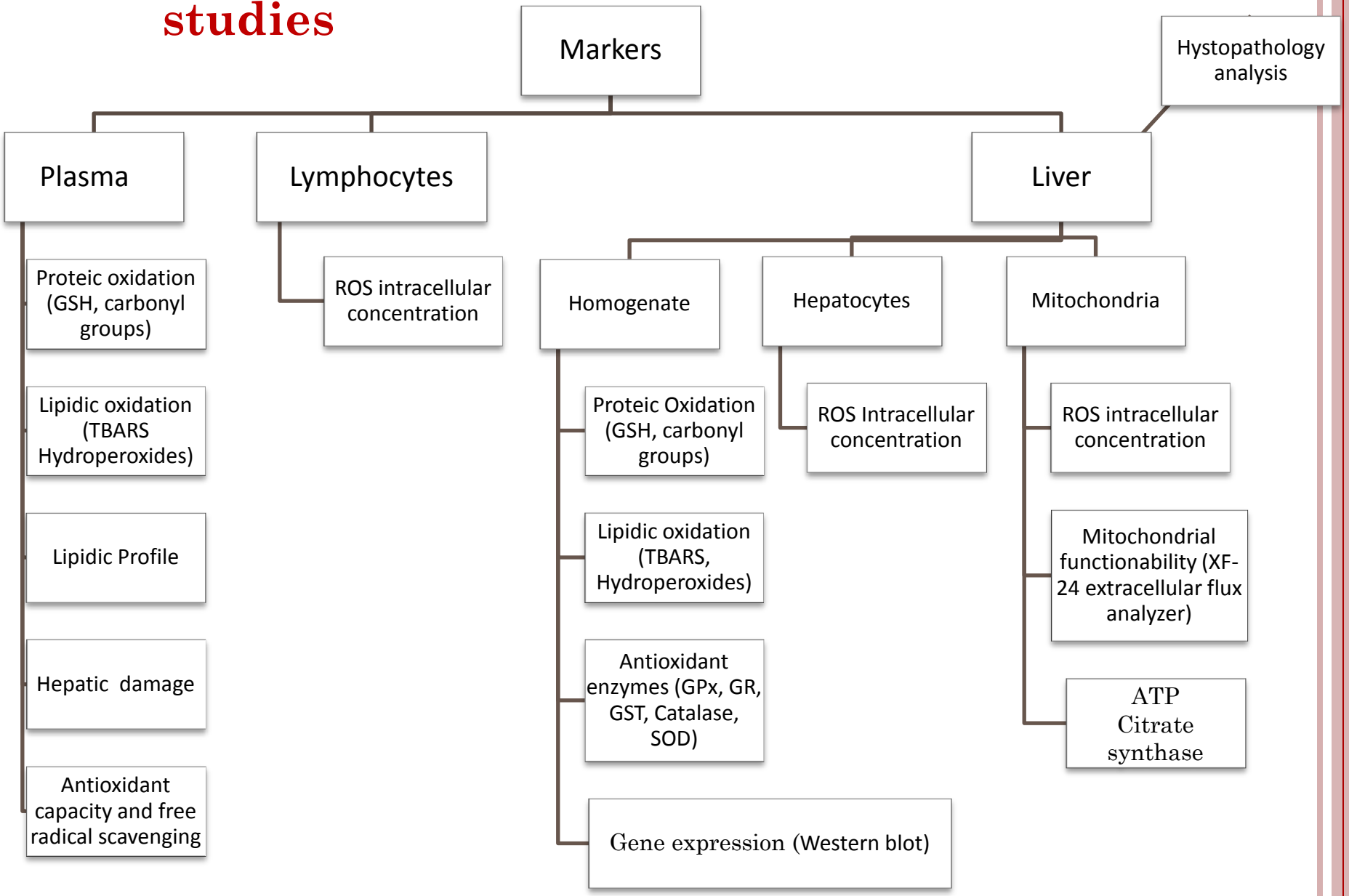
ON ANIMALS studies

(Young and old Wistar rats)



ON ANIMALS studies

(Young and old Wistar rats)



ON ANIMALS studies (Young and old Wistar rats)

PLASMA:

- ✓ Improvement of protein and lipid oxidation markers;
- ✓ Improvement of lipidic profile;
- ✓ Attenuation of hepatic damage markers;
- ✓ Decrease of ROS levels.

LIVER:

- ✓ Improvement of protein and lipid oxidation markers;
- ✓ Increase of antioxidant enzymes;
- ✓ Decrease of ROS levels in hepatocytes.

LIVER MITOCHONDRIA:

- ✓ Increase of ATP and cytrate synthase levels;
- ✓ Decrease of ROS levels;
- ✓ Increase of mitochondrial respiration rate;
- ✓ Increase of vitamin E levels.

ON HUMANS studies

Contents lists available at ScienceDirect

Food Chemistry

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

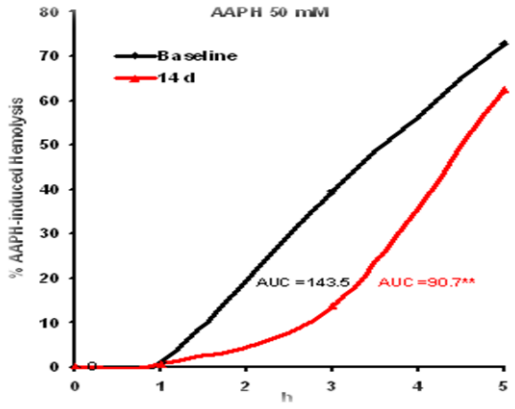
Strawberry consumption improves plasma antioxidant status and erythrocyte resistance to oxidative haemolysis in humans

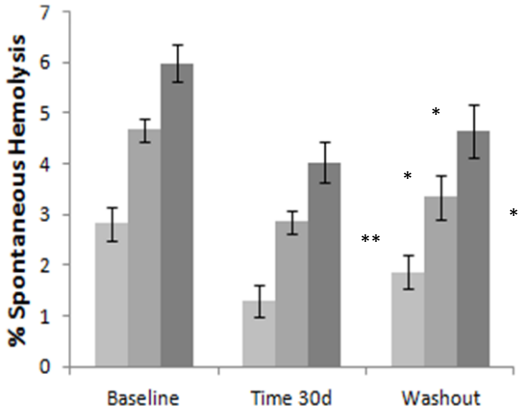
Sara Tulipani [a,1], Josè M. Alvarez-Suarez [a], Franco Busco [b], Stefano Bompadre [c], Josè L. Quiles [d], Bruno Mezzetti [e], Maurizio Battino [a,*]

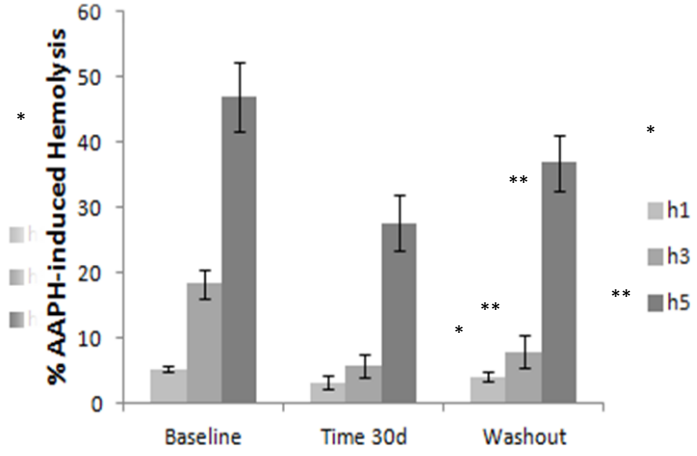
Subjects started a 30-day supplementation period with the consumption of 500 g of fresh strawberries per day

AFTER STRAWBERRY INTAKE

An improved resistance to hemolysis was observed after 30 days of strawberry supplementation and 15 days after the end of the study







ON HUMANS studies

Contents lists available at ScienceDirect

Food Chemistry

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

Strawberry intake increases blood fluid, erythrocyte and mononuclear cell defenses against oxidative challenge

Sara Tulipani [a,1], Tatiana Armeni [a], Francesca Giampieri [a,2], José M. Alvarez-Suarez [a], Ana M. Gonzalez-Paramás [b], Celestino Santos-Buelga [b], Franco Busco [c], Giovanni Principato [a], Stefano Bompadre [d], José L. Quiles [e], Bruno Mezzetti [f], Maurizio Battino [a,*]

Subjects started a 2-week supplementation period with the consumption of 500 g of fresh strawberries per day

AFTER STRAWBERRY INTAKE

Significant reduction in DNA damage (Comet assay) of lymphocytes exposed to oxidative stress, after strawberry consumption

	Control (untreated cells)		H_2O_2-treated cells	
	Baseline	2-week STW	Baseline	2-week STW
Comet Area (μm²)	930.6±29.3	924.9±31	8795.6±397.7	2775±110.4**
Comet Length (μm)	48.2±1.2	50.1±1.6	148.1±33.4	102.6±4.4*
Head Area (μm²)	754.3±22.4	775.1±11.2	1881.5±264.9	370.2±19.5**
Tail Area (μm²)	176.4±27.2	189.8±37.2	6914±122.5	2404.9±124.2**

ON HUMANS studies

ScienceDirect
Journal of Nutritional Biochemistry 25 (2014) 289–294
Journal of Nutritional Biochemistry

One-month strawberry-rich anthocyanin supplementation ameliorates cardiovascular risk, oxidative stress markers and platelet activation in humans☆

José M. Alvarez-Suarez[a], Francesca Giampieri[a,b], Sara Tulipani[c], Tiziana Casoli[d], Giuseppina Di Stefano[e], Ana M. González-Paramás[f], Celestino Santos-Buelga[f], Franco Busco[g], Josè L. Quiles[h], Mario D. Cordero[i], Stefano Bompadre[j], Bruno Mezzetti[b], Maurizio Battino[a,*]

Subjects started a 30-day supplementation period with the consumption of 500 g of fresh strawberries per day

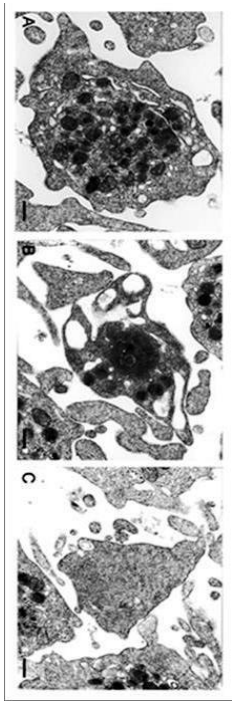
AFTER STRAWBERRY INTAKE

FRAP	↑
ORAC	↑
Vit C	↑
Uric Acid	→

MDA	↓
8-OHdG	↓
Isoprostane	↓

LDL-C	↓
Total Cholesterol	↓
Triglycerides	↓

Function of the protein	Protein name	Accession n° NCBI
Lipid metabolism and transport	Apolipoprotein A-I preproprotein	gi4557321
	Apolipoprotein A-II preprotein	gi4502149
	Apolipoprotein A-IV precursor	gi93163358
	Apolipoprotein C-III precursor	gi4557323
	Apolipoprotein E precursor	gi4557325
	Clusterin isoform 2 (Apo J)	gi42740907
Blood coagulation	Plasminogen	gi4505881
	Fibrinogen beta chain preproprotein	gi70906435
	Fibrinogen, alpha polypeptide isoform alpha-E preproprotein	gi4503689



A) Resting platelet

B) Central clustering platelets

C) Degranulated platelets

ON HUMANS studies

ELSEVIER

ScienceDirect

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Journal of Nutritional Biochemistry

One-month strawberry-rich anthocyanin supplementation ameliorates cardiovascular risk, oxidative stress markers and platelet activation in humans☆

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Subjects started a 30-day supplementation period with the consumption of 500 g of fresh strawberries per day

The American Journal of Clinical Nutrition

Anthocyanin supplementation improves serum LDL- and HDL-cholesterol concentrations associated with the inhibition of cholesteryl ester transfer protein in dyslipidemic subjects[1–4]

Yu Qin, Min Xia, Jing Ma, YuanTao Hao, Jing Liu, HaiYing Mou, Li Cao, and WenHua Ling

Am J Clin Nutr 2009;90:485–92.

Circulation

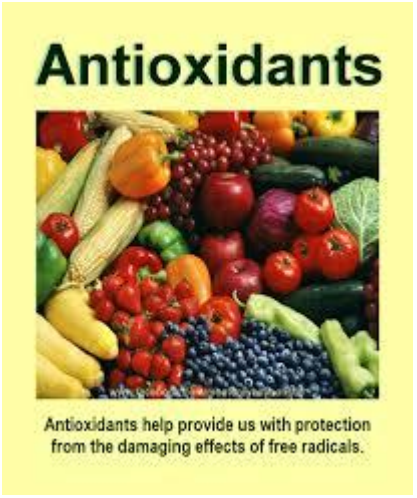
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association.

High Anthocyanin Intake Is Associated With a Reduced Risk of Myocardial Infarction in Young and Middle-Aged Women

Aedín Cassidy, Kenneth J. Mukamal, Lydia Liu, Mary Franz, A. Heather Eliassen and Eric B. Rimm

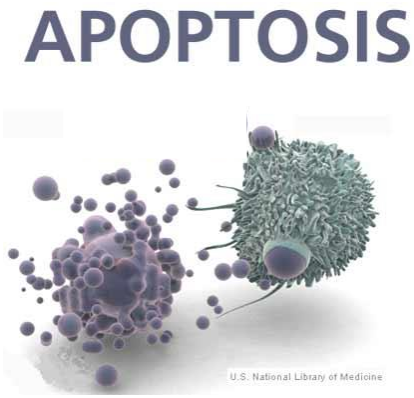
Circulation. 2013;127:188-196
doi: 10.1161/CIRCULATIONAHA.112.122408



Until today, berries in general were considered to be a rich-natural source of bioactive compounds (mainly polyphenols) with antioxidant properties..

BUT

…..polyphenols don't have only antioxidant properties. They also display other effects, like pro-apoptotic or pro-oxidant effects, that may seem negative but in hyperproliferative cells can have, in turn, positive effects



IN VITRO studies

Cancer cells

Murine mammary tumoral cell lines

N202/1A

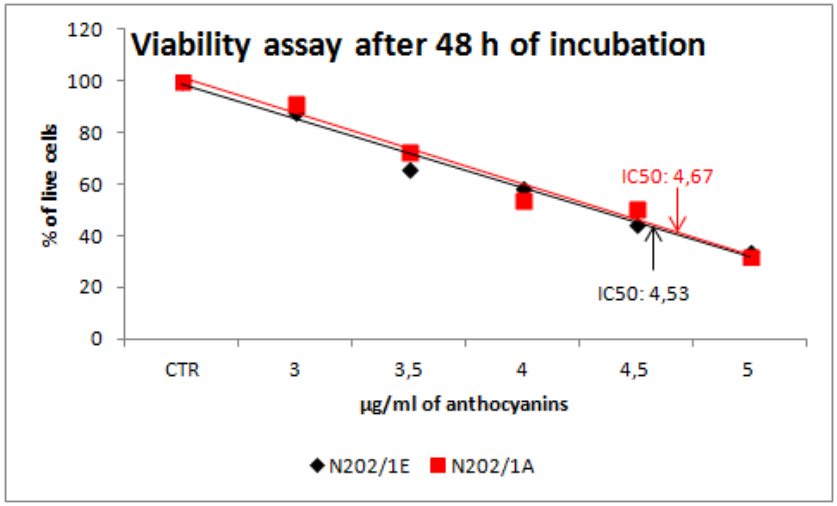
High levels of HER 2/neu oncoprotein expression

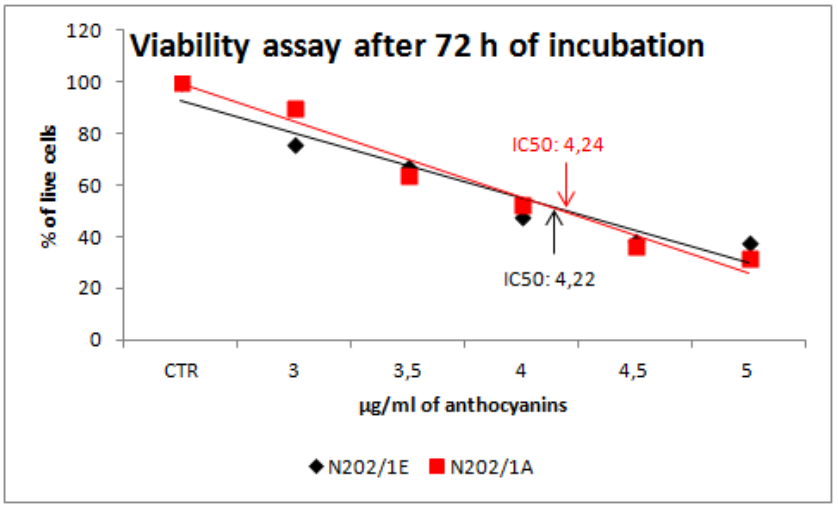
N202/1E

No detectable HER 2/neu oncoprotein expression

Treated with different concentrations of strawberries methanolic extracts

Cell viability

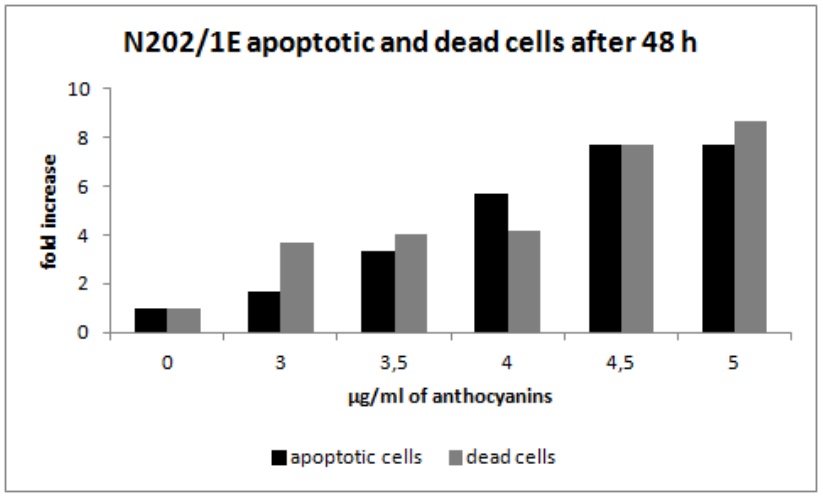


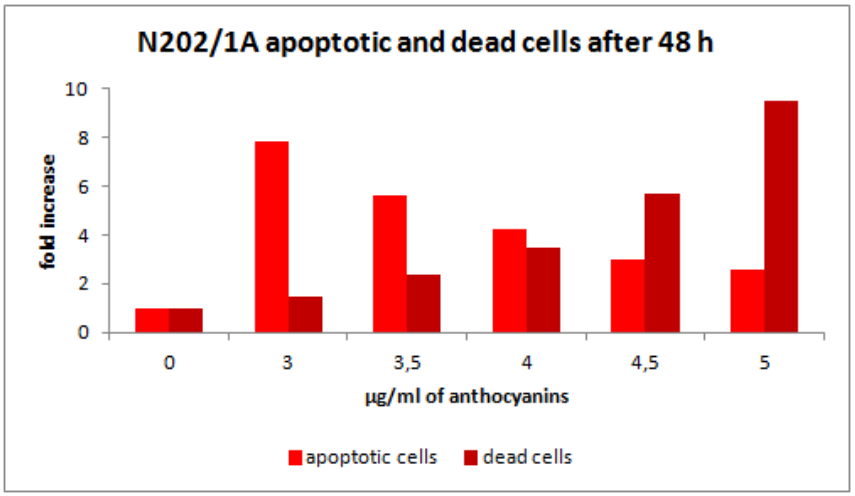


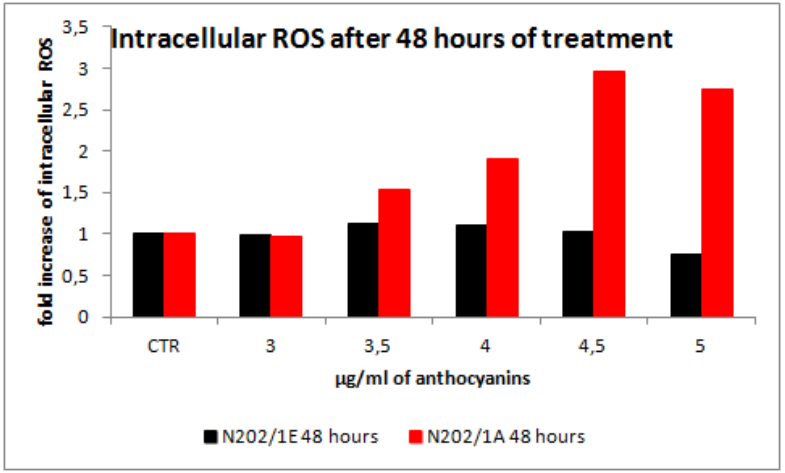
IN VITRO studies
Cancer cells

Murine mammary tumoral cell lines

Apoptosis rate and intracellular ROS concentration after 48 hours of incubation with strawberry methanolic extracts.



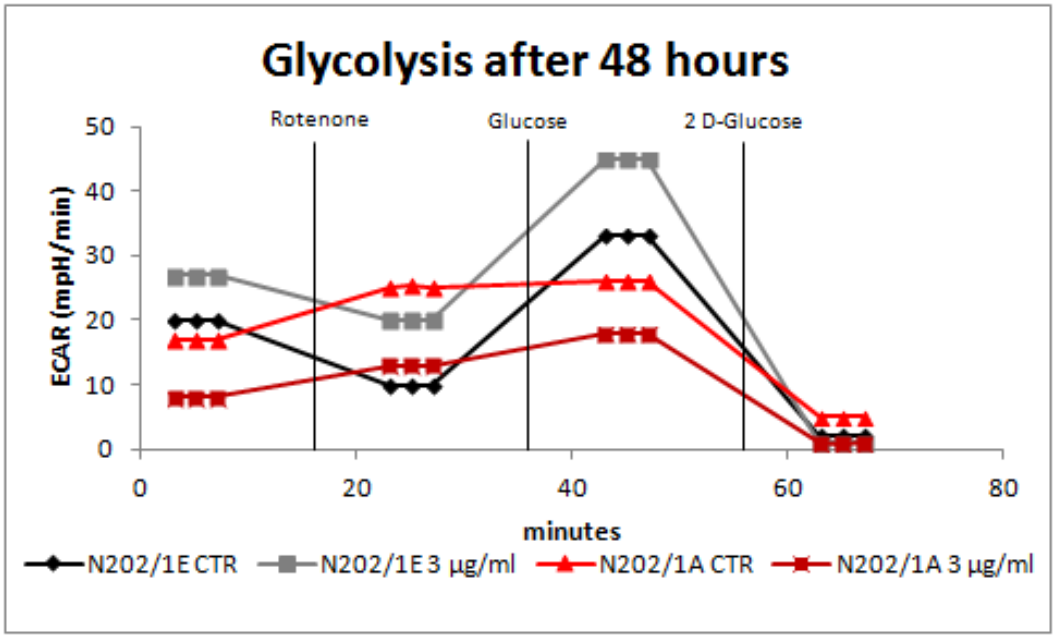




IN VITRO studies
Cancer cells

Murine mammary tumoral cell lines

Seahorse XF-24 : Glycolysis at different concentrations of strawberry extracts

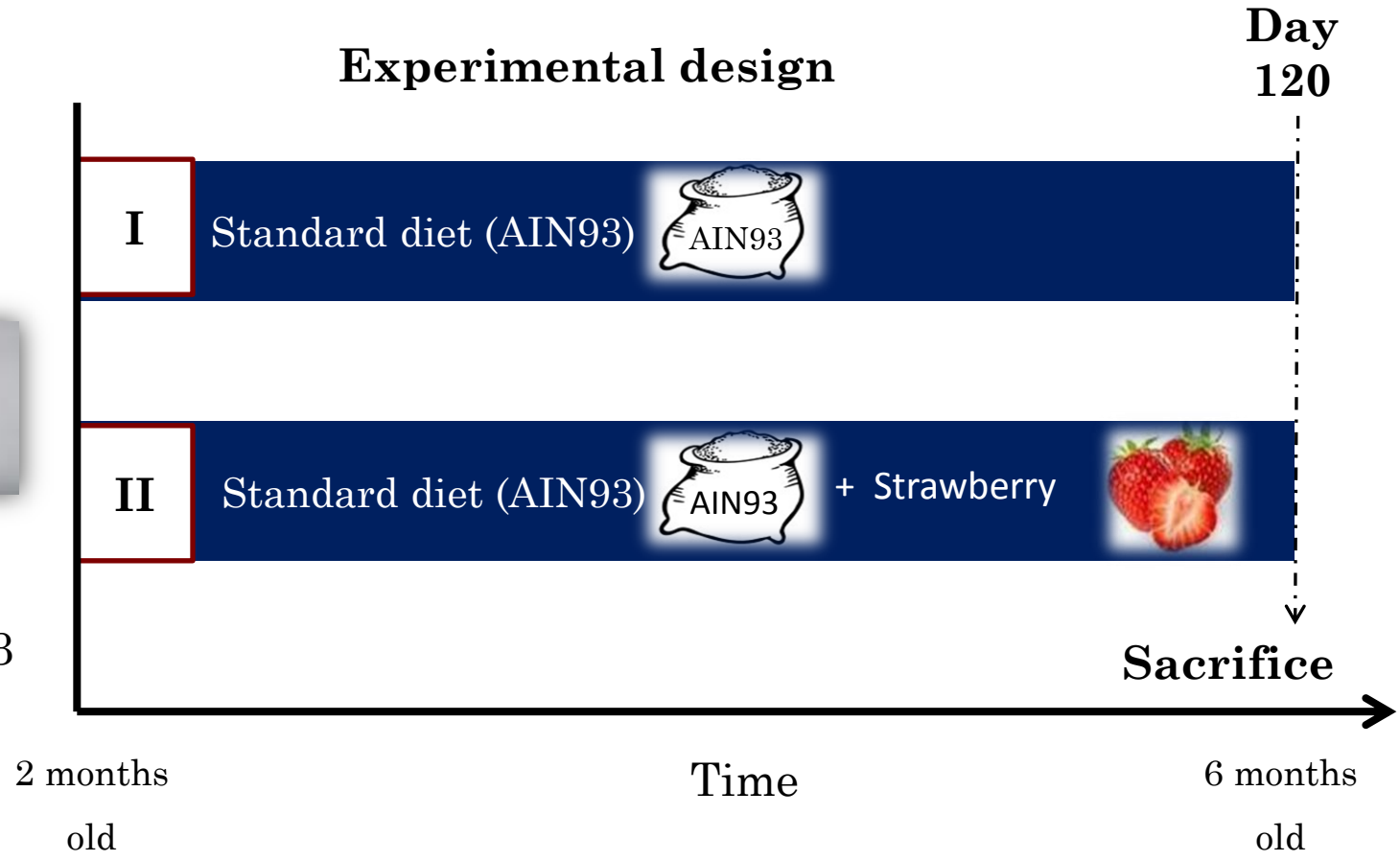


- N202/1E respond to glycolysis inhibitors better than N202/1A;
- Strawberry treatment (for example 3 µg/ml of anthocyanins) is capable to increase the glycolysis in N202/1E, but decreases glycolysis in N202/1A.

IN VITRO studies
Cancer cells

Murine line FVB/N 233 neu-NT

Murine line FVB/N 233 neu-NT



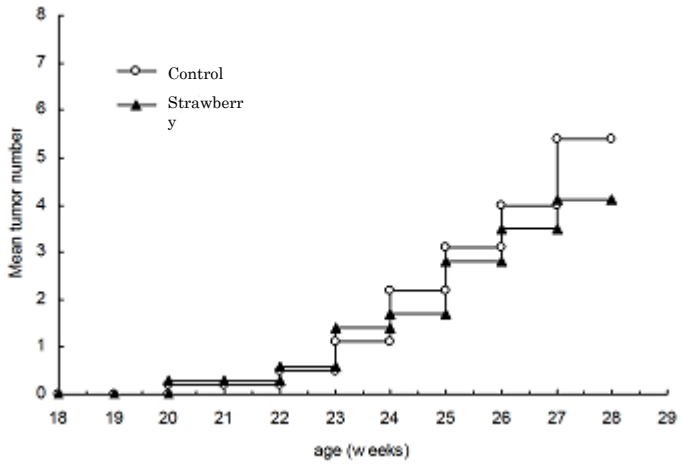
- Kinetics of breast cancer development
- Lung metastases formation

IN VITRO studies
Cancer cells

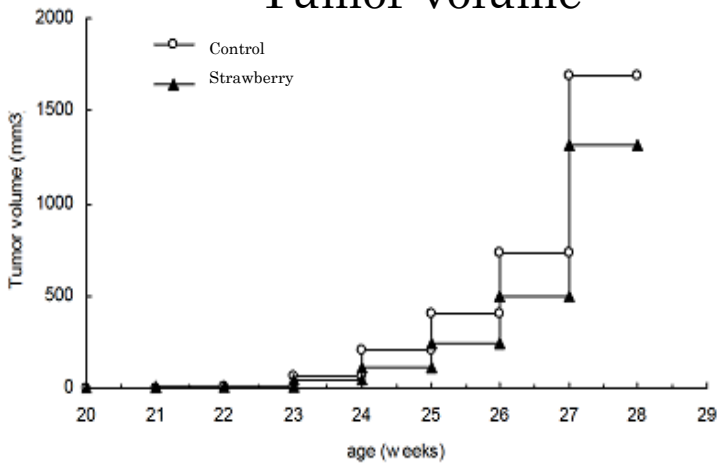
Murine line FVB/N 233 neu-NT

Kinetics of cancer development

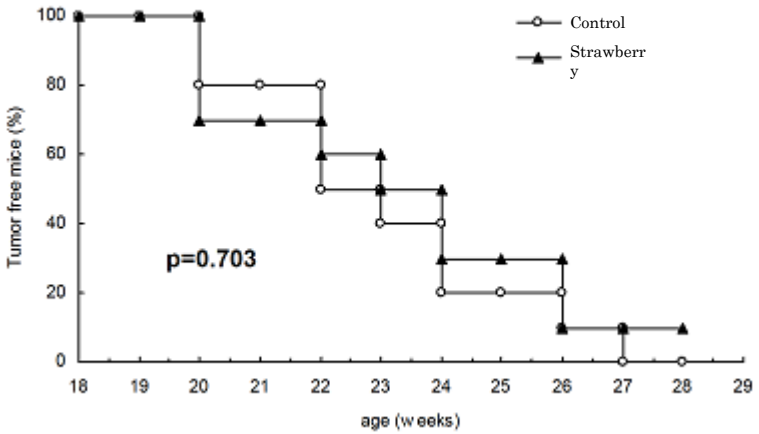
Tumor number



Tumor volume



Tumor free mice



IN VITRO studies
Cancer cells

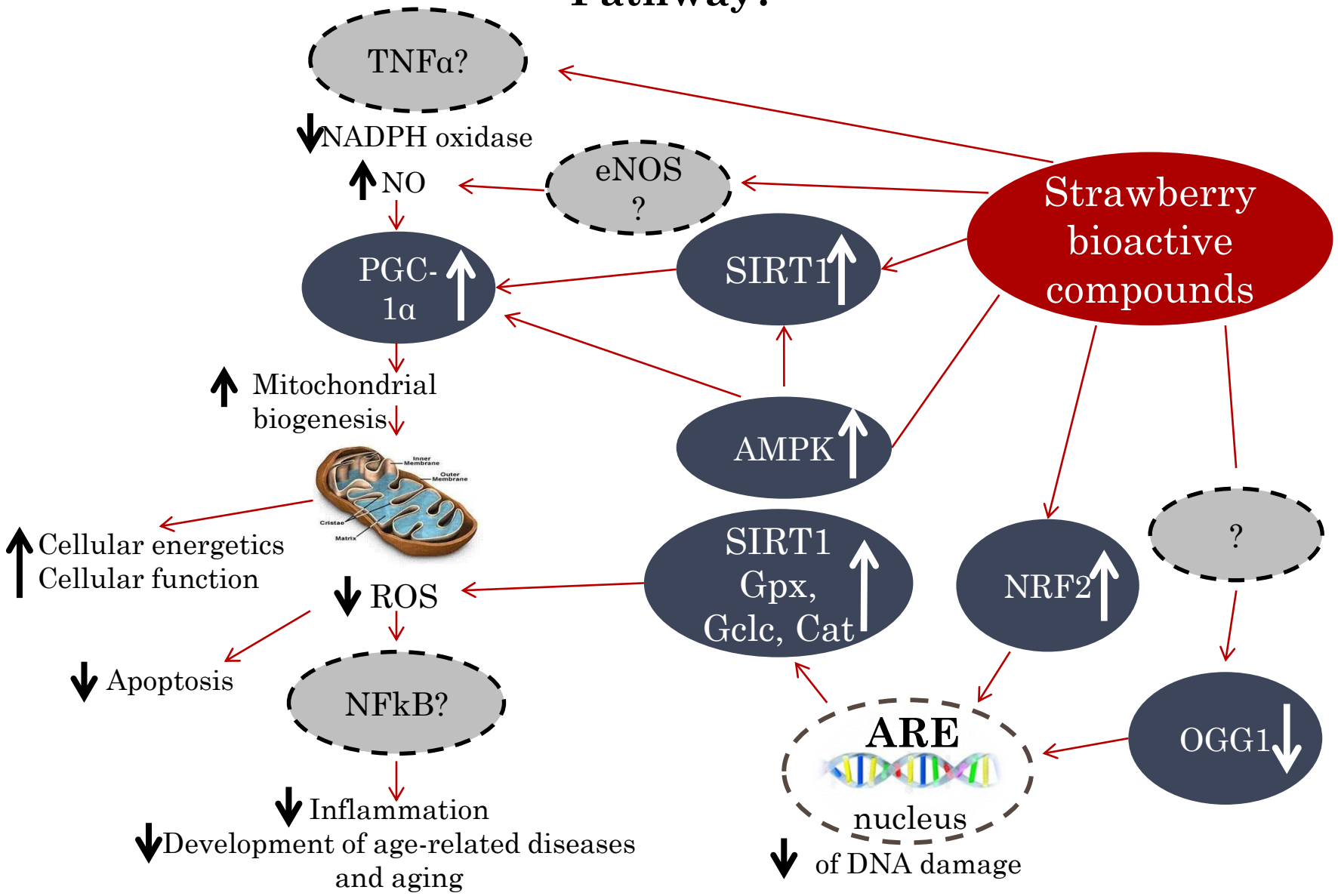
Murine line FVB/N 233 neu-NT

Lung metastases formation:

- Metastases number
- % mice with metastases
- Metastases size

	Control (10 animals)	Strawberry (10 animals)
Lung metastases		
Mean no. of metastases	0.33	0
Mice with metastases (%)	33.3	0
Mean size of metastases (mm)	1.33	0
Maximum size of metastases (mm)	2	0

Could strawberries protect against oxidative damage through direct or Indirect activation of the SIRT 1/PGC 1α/NRF 2 Pathway?



Evidences for strawberry health benefits
- Take home messages -

Characterization of the main bioactive compounds and of their antioxidant capacity

Strawberry treatment

In vitro

- Protection against UV irradiation in human fibroblasts;
- Improvement of mitochondrial respiration and glycolysis after H_2O_2- and AAPH-induced stress in human fibroblasts.

- Inhibition of viability, increase of apoptosis and intracellular ROS production and impairment of mitochondrial functionality in murine breast cancer cells.

In vivo

- Improved resistance of erythrocytes to hemolysis;
- Improvement of oxidative stress biomarkers and lipid profile in plasma;
- Reduced DNA damage in lymphocytes after H_2O_2-induced stress.

- Protection against ethanol-induced gastric lesions;
- Reduction of breast tumor number and volume and lung metastases;
- Improvement of antioxidant status and mitochondrial functionality against DOX-induced stress.

SOCIAL IMPACT

Mail Online

Time for a daiquiri? Strawberries can protect your stomach from harmful effects of alcohol

Drink easy: A diet rich in strawberries can protect the stomach from alcohol, according to scientists

INDIA TODAY GROUP : India Today | Aaj Tak | Headlines Today | Business Today | Men's Health | Wonder Wom

Updated 16:29 IST | July 11, 2013

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India Today / Lifestyle / Health / Story

IANS MADRID, AUGUST 6, 2012 | UPDATED 16:39 IST

Strawberry extract protects skin against UV rays

TAGS: Strawberry extract | UV rays | Skin cells | Ultraviolet radiation

RELATEDS

- Protect skin with sunscreen, but use lightly
- Beat the summer- sleep well, eat well for glowing skin

BOAS NOTÍCIAS

Um mundo em crescimento

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Quinta-feira, 27 de Fevereiro de 2014

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Strawberries and cream: Sun lotion made from popular fruit could be more effective

By DAILY MAIL REPORTER

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STRAWBERRIES can lower levels of cholesterol and harmful blood fat - if you eat enough of them, research has shown.

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Des fraises contre le cholestérol

Mots clés : fraise, cholestérol, maladie cardiovasculaire

Par Anne-Laure Lebrun - le 04/03/2014

Une nouvelle étude confirme que manger des fraises aide à lutter contre le chostérol et protégerait des maladies cardiovasculaires.

Des chercheurs britanniques avaient récemment cherché à établir la véracité du proverbe **«une pomme chaque matin éloigne le médecin»**. Il pourrait en être de même pour **les fraises**, selon une nouvelle **étude italo-espagnole.**

Manger des fraises plusieurs fois dans le semaine protègerait des maladies cardiovasculaires.

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