The effects of strawberry bioactive compounds on lipid metabolism and adipogenesis

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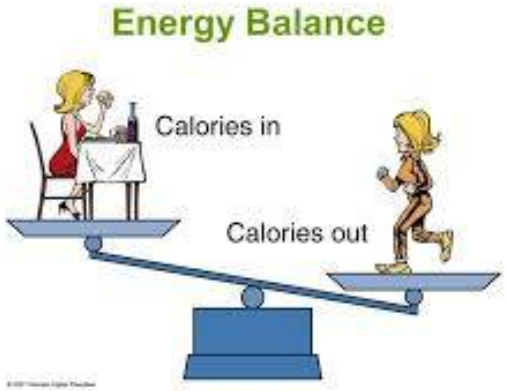
Highly Cited Researcher 2019 — Web of Science Group

Highly Cited Researcher 2020 — Clarivate

HOW CAN OBESITY BE DEFINED?

OBESITY is defined as abnormal or excessive fat accumulation that may impair health.

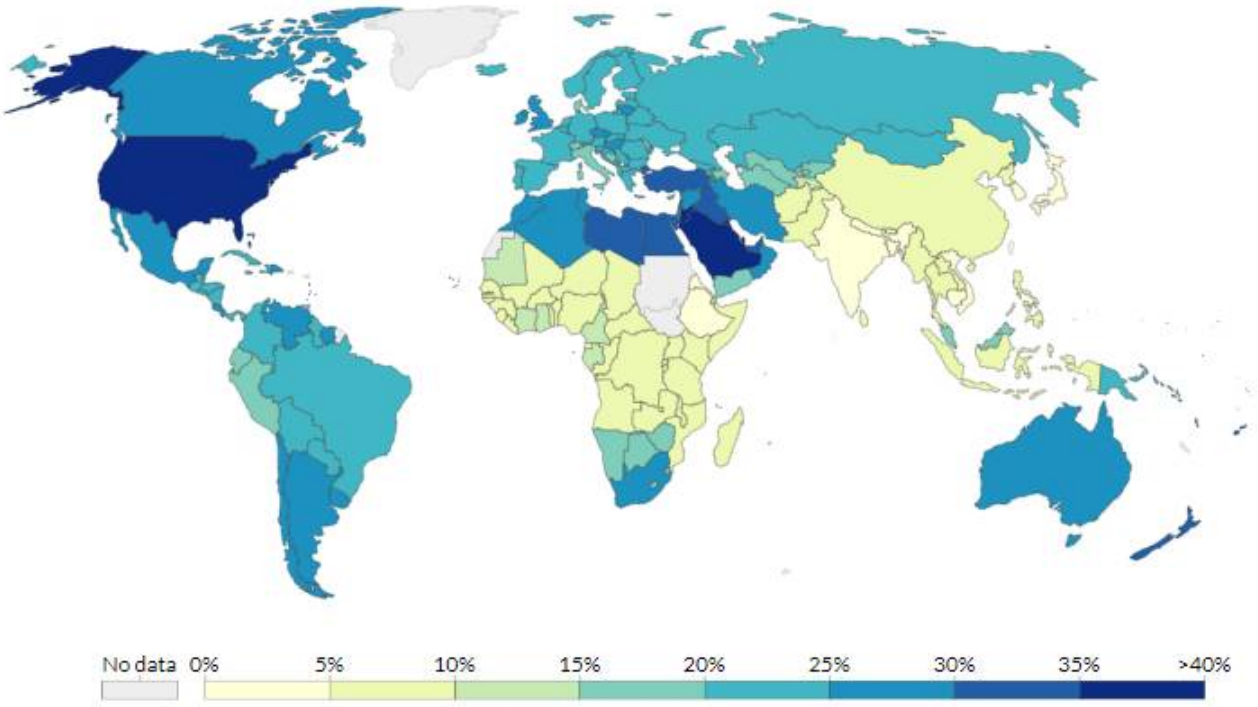
The fundamental cause of obesity and overweight is an energy imbalance between calories consumed and calories expended.



OVERWEIGHT AND OBESITY IN THE WORLD

World Health Organization

Percentage of adults who are defined obese according to their BMI, 2016

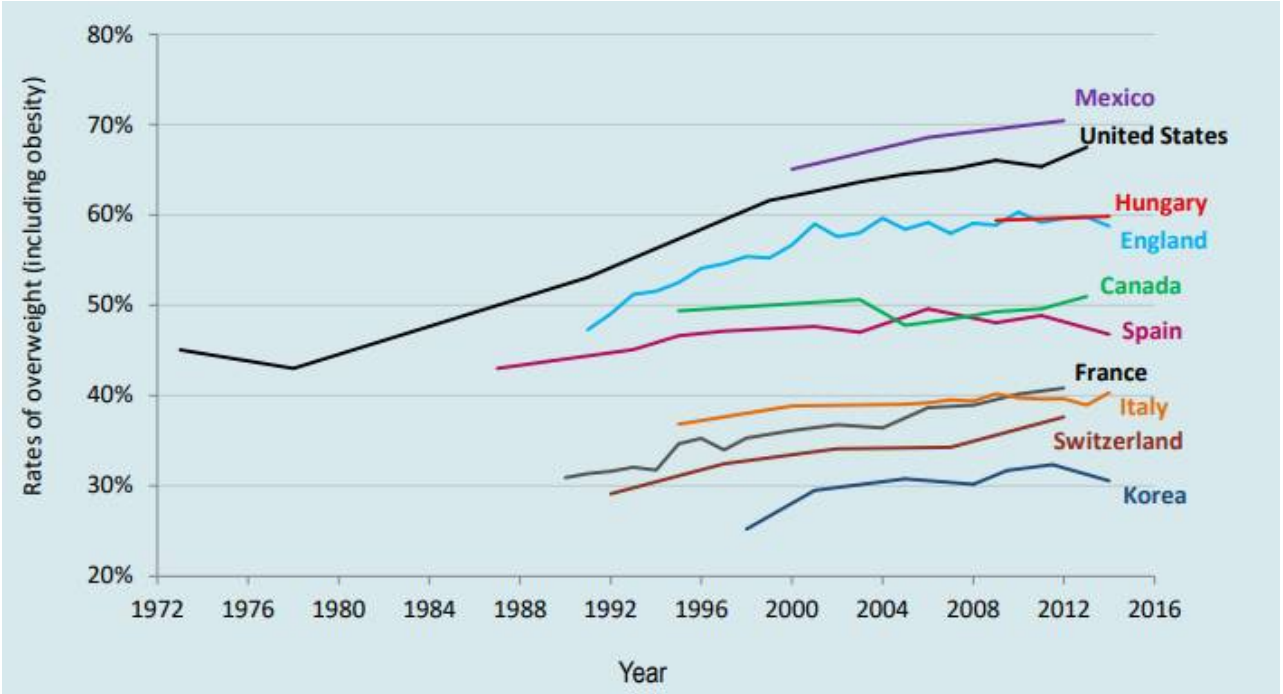


Source: WHO, Global Health Observatory

Most of the world's population live in a country where there are more people overweight and obese than underweight.

OVERWEIGHT AND OBESITY TRENDS IN THE WORLD

Rising overweight (including obesity) rates in adults aged 15 -74 years

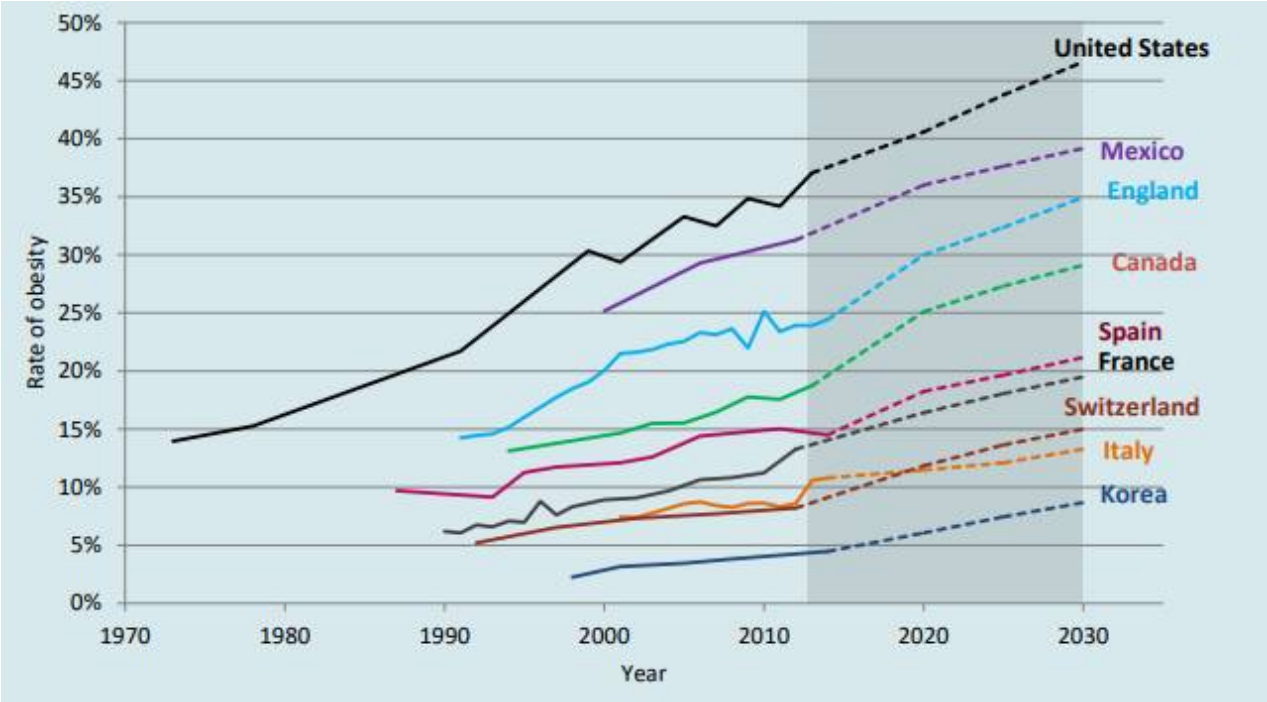


OBESITY RATES ARE EXPECTED TO INCREASE FURTHER

World Health Organization

OVERWEIGHT AND OBESITY TRENDS IN THE WORLD

Rising overweight (including obesity) rates in adults aged 15 -74 years

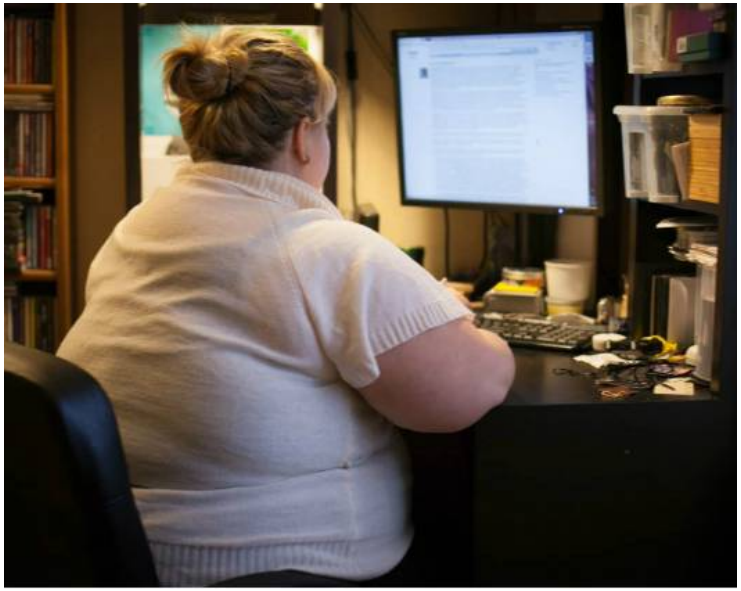


OBESITY RATES ARE EXPECTED TO INCREASE FURTHER

World Health Organization

FACTS ABOUT OVERWEIGHT AND OBESITY

More than 1.9 billion adults were overweight in 2016 and 650 million obese



- In 2016, more than 1.9 billion adults were overweight and 650 million were obese.
- At least 2.8 million people each year die as a result of being overweight or obese.
- The prevalence of obesity nearly tripled between 1975 and 2016.
- Once associated with high-income countries, obesity is now also prevalent in low- and middle-income countries.

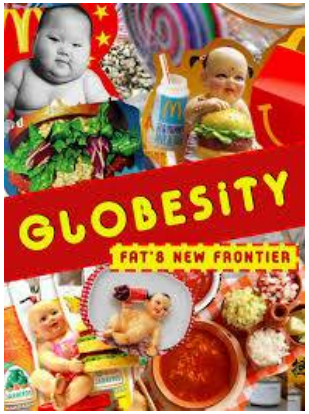
By 2025 it is estimated that 2.7 billion adults and 268 million school-age children will be overweight or obese

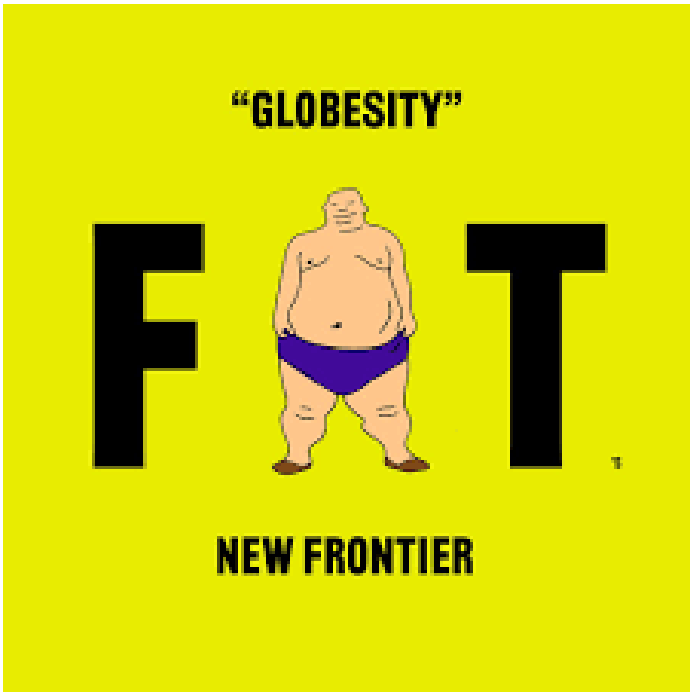
FACTS ABOUT OVERWEIGHT AND OBESITY

Globally, 41 million preschool children were overweight in 2016

- Overweight children are likely to become obese adults.
- They are more likely than non-overweight children to develop diabetes and CVDs at a younger age, which in turn are associated with a higher chance of premature death and disability.

Childhood obesity is one of the most serious public health challenges of the 21st century.





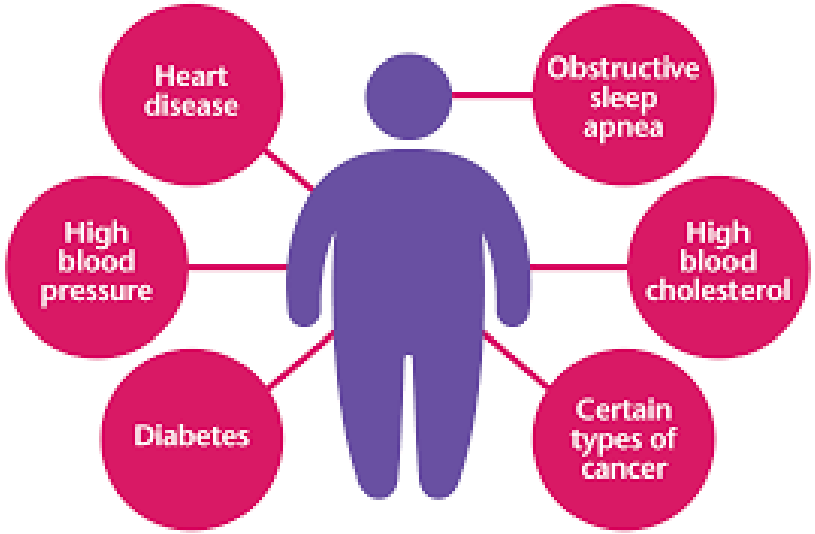
Obesity is a pandemic!!!!

FACTS ABOUT OVERWEIGHT AND OBESITY

Global Disability-Adjusted Life-Years and Deaths Associated with a High Body-Mass Index (2015)

The Consequences Of Obesity

- Coronary heart disease
- Type 2 diabetes
- Cancer (endometrial, breast, colon)
- Hypertension
- Stroke
- Liver disease
- Sleep apnea and respiratory problems
- Osteoarthritis
- Gynecological problems (abnormal menses, infertility)



OVERWEIGHT AND OBESITY ARE LINKED TO MORE DEATHS WORLDWIDE THAN UNDERWEIGHT

Risk factors of obesity

Prevalence wi
Age

Due to Medications
Medical Problems

Lack of Sleep
Sleep Deprivation

Being
Physically Inactive

Impact of Socio
Economic factors

Consuming
Unhealthy Diet

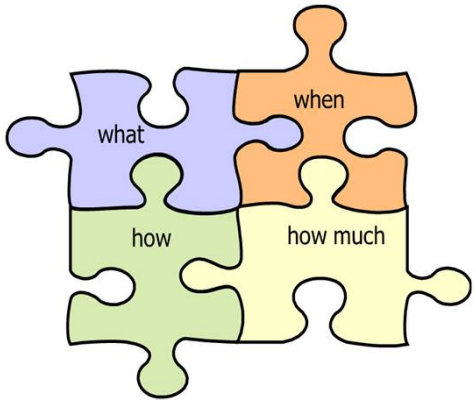
Impact of
Psychological factors

With Family
Lifestyle & **Habits**

Role of
Genetics

https://mumsfertility.com/overweight-obesity-causes-symptoms/

Health and nutrition

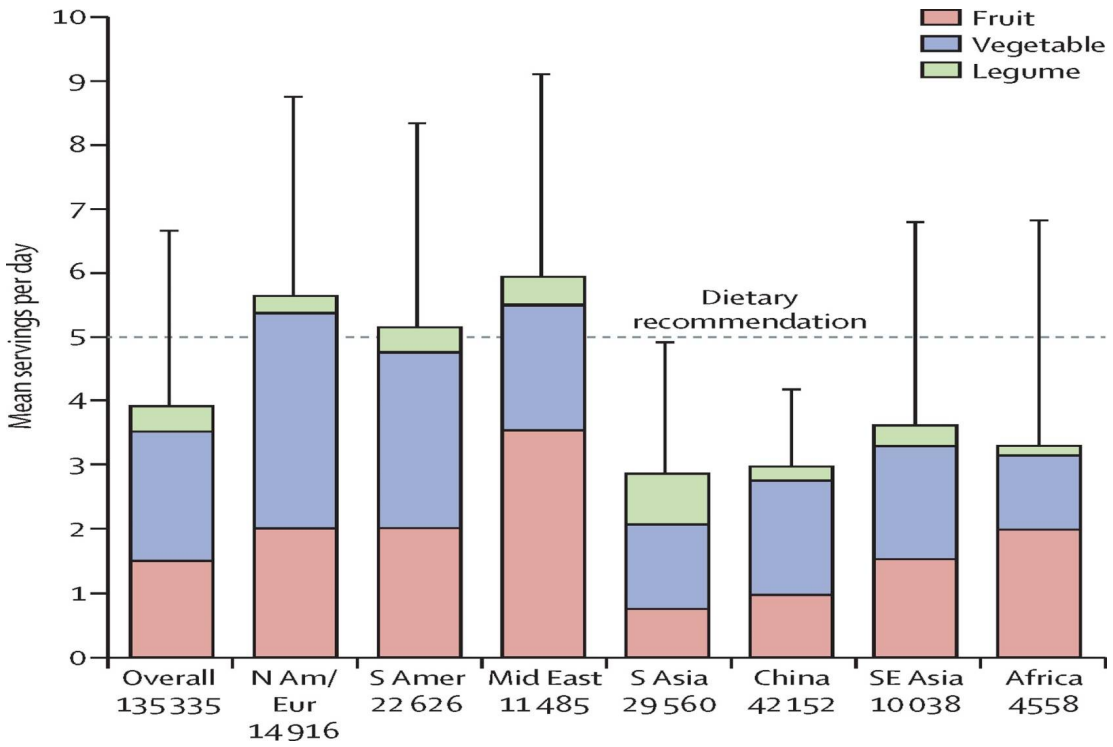


- Modernization
- Urbanization
- Demographic changes
- Socio-economic changes/economic growth
- Globalization of the world food market
- Media, marketing

Increased intake of calorie rich, low nutritive value foods: high intake of fats, trans fats, sugar, salt.

Health and nutrition

THE LANCET
Volume 390, Issue 10107, 4–10 November 2017, Pages 2037-2049



FRUIT AND VEGETABLE PROMOTION INITIATIVE / A MEETING REPORT / 25-27/08/03

- Up to 2.7 million lives could be saved annually with sufficient fruit and vegetable consumption.
- Low fruit and vegetable intake is among the top 10 selected risk factors for global mortality.

2.5 THE "5 A DAY PROGRAM" IN THE UNITED STATES OF AMERICA

Dr Lorelei DiSogra, Director, 5 A Day For Better Health Program, National Cancer Institute, Dr Frances Taccone, Director of Development, Produce for Better Health Foundation

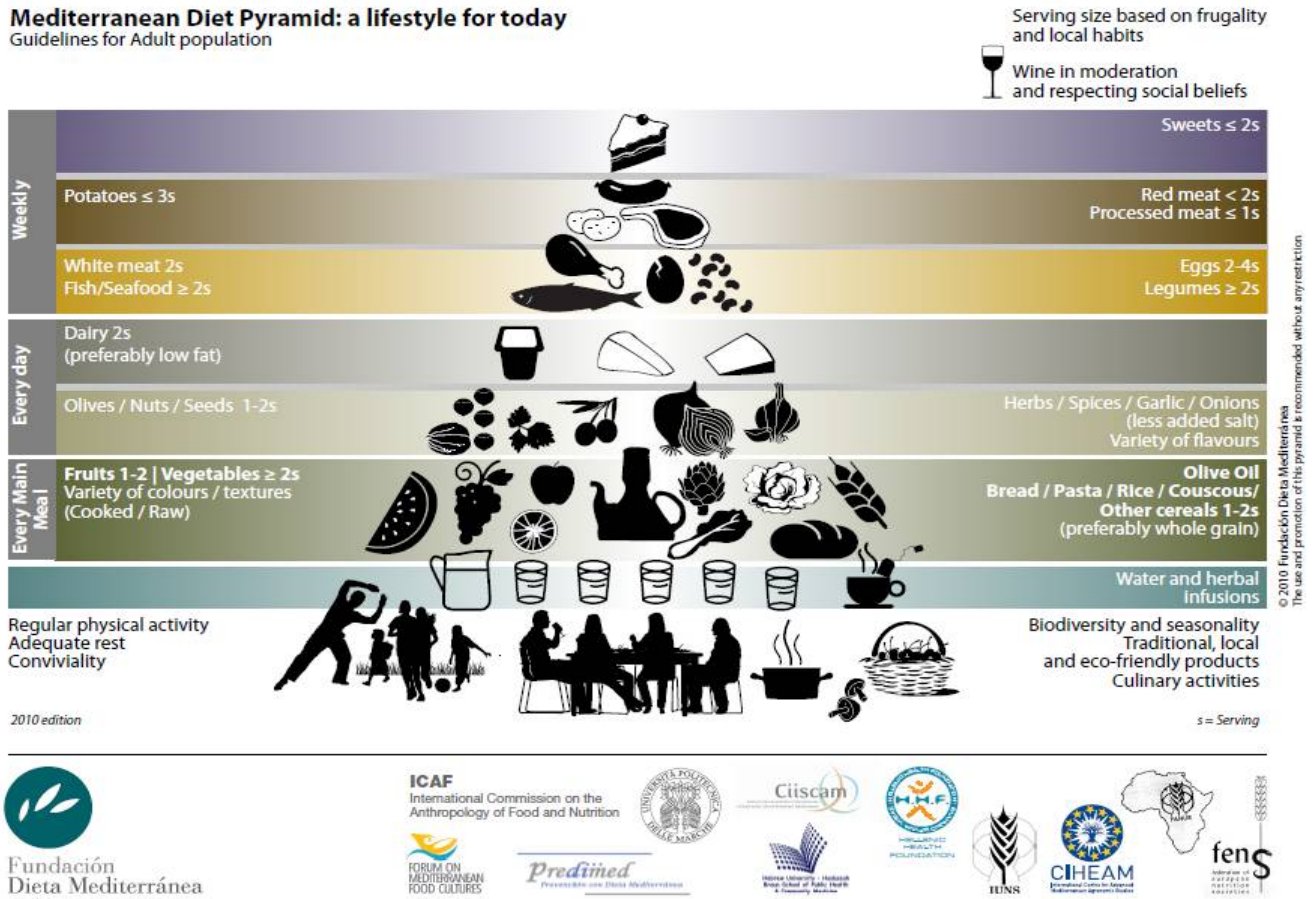
2.6 THE EUROPEAN 5 A DAY-TYPE PROGRAMMES

Morten Strunge Meyer, Danish Cancer Society

2.7 SETTING UP A FRUIT AND VEGETABLE PROMOTION INITIATIVE IN A DEVELOPING COUNTRY

Dr Carlos A Monteiro, Centre for Epidemiological Studies in Health and Nutrition, School of Public Health, University of Sao Paulo

Mediterranean diet:
a tool for primary prevention



Public Health Nutrition: 14(12A), 2274–2284 doi:10.1017/S1368980011002515

Mediterranean diet pyramid today. Science and cultural updates

Maurizio Battino

Bioenergetic Lab

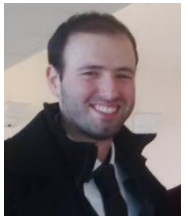
Sara Tulipani

José M.Alvarez-Suárez

Stefania Romandini

Francesca Giampieri

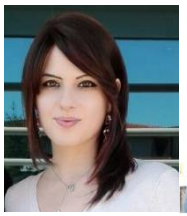
Tamara Y. Forbes-Hernanc



Luca Mazzoni

Massimiliano Gasparrini

Sadia Afrin



Danila Cianciosi

Alfonso Varela Lopez

Jiaojiao «JoJo» Zhang

Johura Ansary

In the last 25 years...

- Nutritional and phytochemical characterization
- *In vitro* studies of anti-inflammatory, antitumor, antioxidant, and anti-atherosclerotic effects in various cellular models.
- *In vivo* studies with the aim of evaluating the effects on mitochondrial function, oxidative stress as well as on inflammatory, metabolic and apoptotic processes in animals and humans models

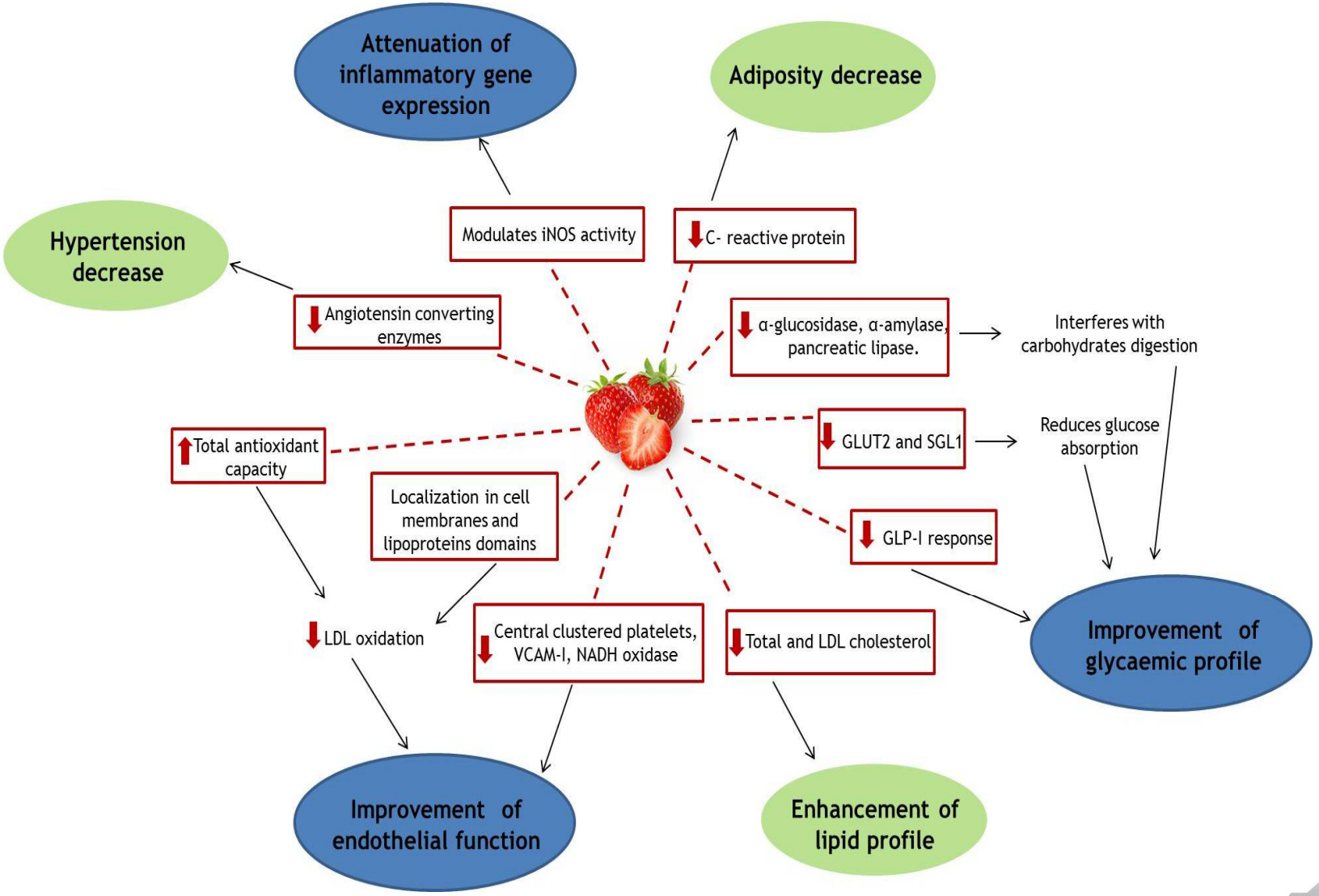
Anti-carcinogenic properties

Anti-inflammatory properties

Our findings...

Lipid-lowering effects

Antioxidant activity


Attenuation of inflammatory gene expression
Adiposity decrease
Hypertension decrease
Modulates iNOS activity
C- reactive protein
Angiotensin converting enzymes
α-glucosidase, α-amylase, pancreatic lipase.
Interferes with carbohydrates digestion
Total antioxidant capacity
GLUT2 and SGL1
Reduces glucose absorption
Localization in cell membranes and lipoproteins domains
GLP-I response
LDL oxidation
Central clustered platelets, VCAM-I, NADH oxidase
Total and LDL cholesterol
Improvement of glycaemic profile
Improvement of endothelial function
Enhancement of lipid profile

Strawberry Romina

Bioactive compounds	Values
Total Polyphenols (mg GAeq/g FW)	2.64 ± 2.63
Total Flavonoids (mg CATeq/g FW)	1.02 ± 0.87
Vitamin C (mg /g FW)	0.39 ± 0.23
Cyanidin-3-O-glucoside chloride (mg /g FW)	0.03 ± 0.02
Pelargonidin-3-O-glucoside chloride (mg /g FW)	0.70 ± 0.25
Pelargonidin-3-O-rutinoside chloride (mg /g FW)	0.04 ± 0.08
Tetrahydrofolic acid (ng /g FW)	830.30 ± 5.04
5-methyl tetrahydrofolic acid (ng /g FW)	5.20 ± 1.12

Fraction	FRAP (µmol Txeq/g)	DPPH (µmol Txeq/g)	ABTS (µmol Txeq/g)
Fresh fruit	22.70 ± 2.03	8.11 ± 0.25	10.71 ± 0.58
Dried methanolic extract	168.25 ± 3.95	30.29 ± 0.18	35.51 ± 0.06

Romina: A powerful **strawberry** with in vitro efficacy against uterine leiomyoma cells.

Giampieri F, Islam MS, Greco S, Gasparrini M, Forbes Hernandez TY, Delli Carpini G, Giannubilo SR, Ciavattini A, Mezzetti B, Mazzoni L, Capocasa F, Castellucci M, Battino M, Ciarmela P.

J Cell Physiol. 2019 May;234(5):7622-7633. doi: 10.1002/jcp.27524. Epub 2018 Oct 14.

Strawberry fruit (**Fragaria** x ananassa cv. **Romina**) extenuates iron-induced cardiac oxidative injury via effects on redox balance, angiotensin-converting enzyme, purinergic activities, and metabolic pathways.

Erukainure OL, Salau VF, Oyenihi AB, Mshicileli N, Islam MS.

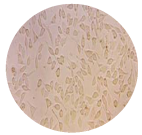
J Food Biochem. 2020 Aug;44(8):e13315. doi: 10.1111/jfbc.13315. Epub 2020 Jun 8.

Strawberry (cv. **Romina**) Methanolic Extract and Anthocyanin-Enriched Fraction Improve Lipid Profile and Antioxidant Status in HepG2 Cells.

Forbes-Hernández TY, Gasparrini M, Afrin S, Cianciosi D, González-Paramás AM, Santos-Buelga C, Mezzetti B, Quiles JL, Battino M, Giampieri F, Bompadre S.

Int J Mol Sci. 2017 May 28;18(6):1149. doi: 10.3390/ijms18061149.

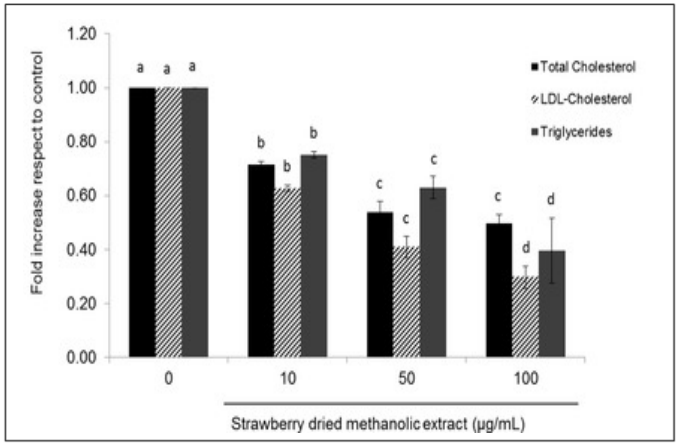
Lipid-lowering properties of strawberry polyphenols



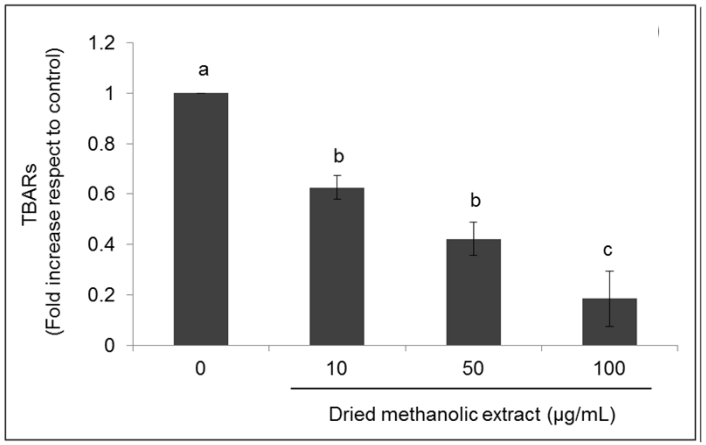
HepG2

Strawberry treatment improves lipid profile and antioxidant status in HepG2 cells

Triglycerides, Total and LDL-cholesterol



Lipid peroxidation



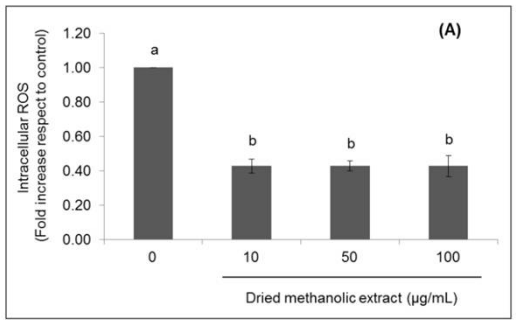
Forbes-Hernandez et al., 2017 Int J Mol Sci, 18, 1149.

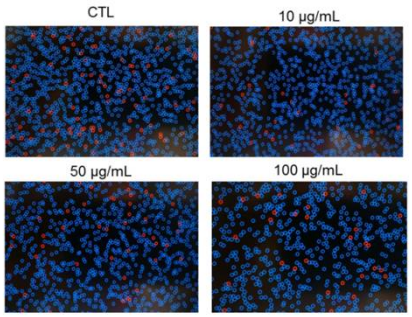
Lipid-lowering properties of strawberry polyphenols

HepG2

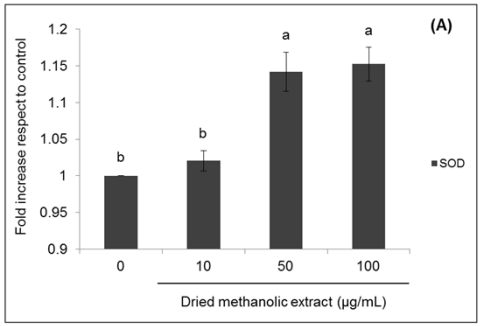
Strawberry treatment improves lipid profile and antioxidant status in HepG2 cells

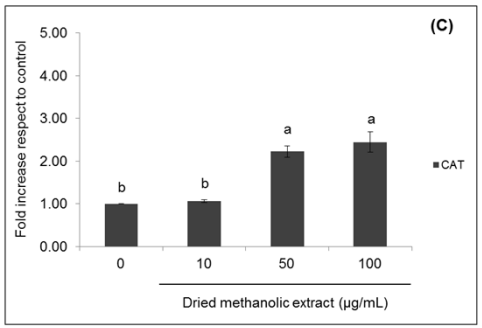
↓ Intracellular ROS production





↑ Antioxidant enzymes activity





Forbes et al., 2017 Int J Mol Sci, 18, 1149.

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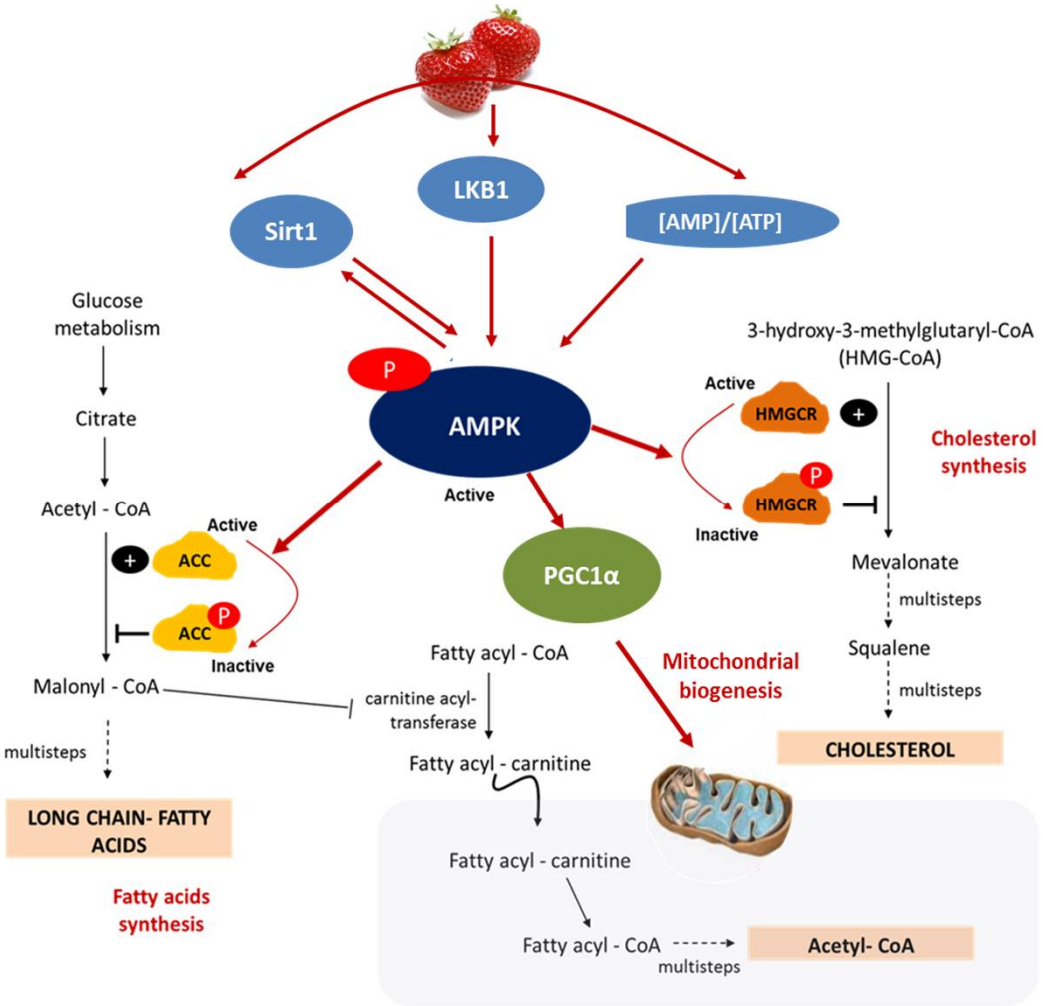

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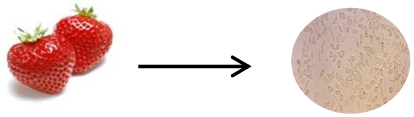
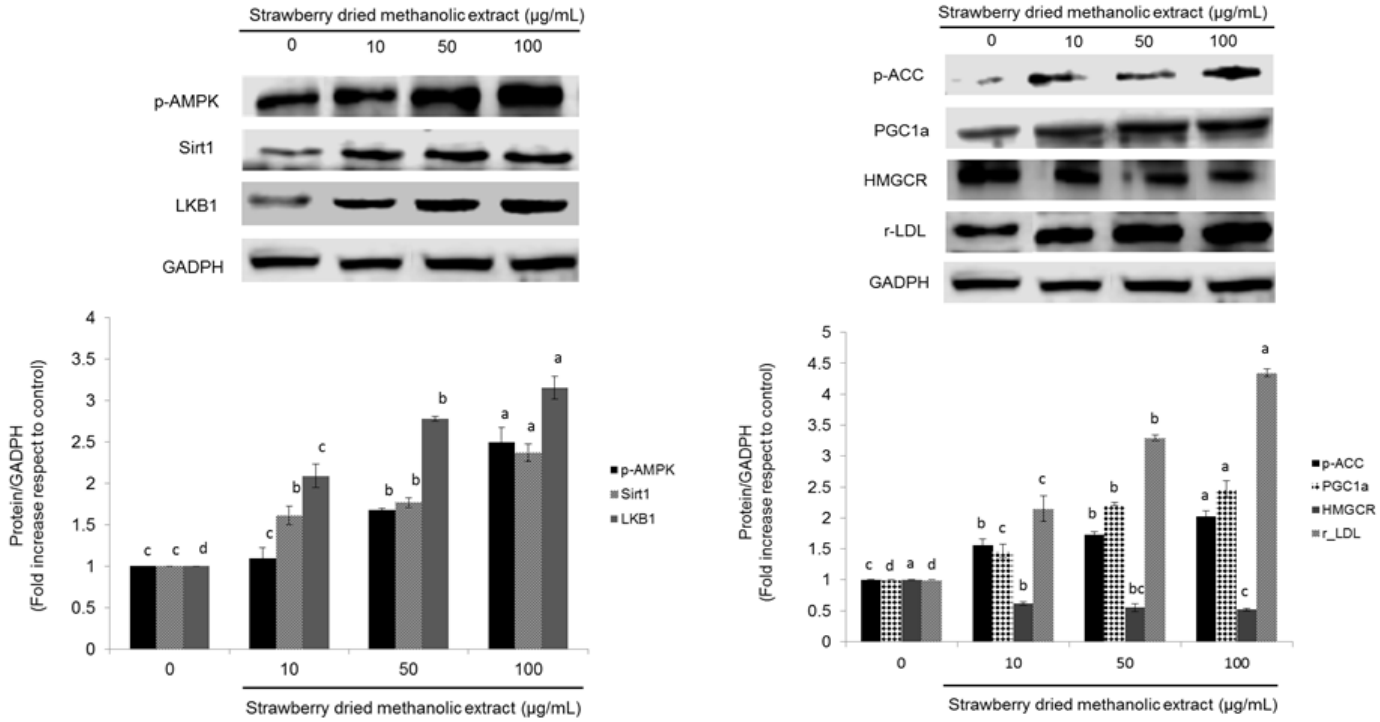


HepG2

Expression of proteins related to the AMPK pathway



Forbes-Hernandez et al., 2017 , Nutrients, 9, 621.

Lipid-lowering properties of strawberry polyphenols

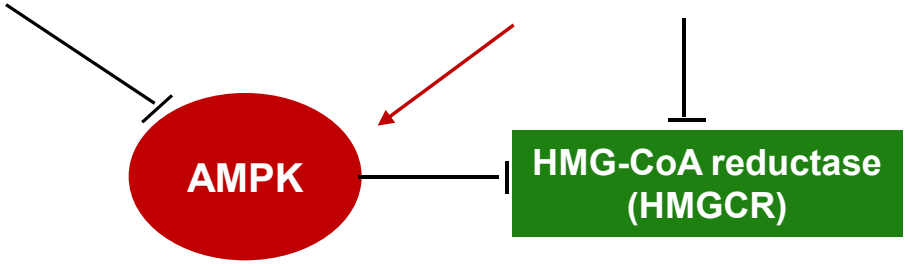
How to confirm the involvement of AMPK pathway in the strawberry mechanisms of action?

COMPOUND C

pharmacological compound with the important function of blocking the phosphorylation of AMPK and, as a consequence, to inactivate this protein.

LOVASTATIN

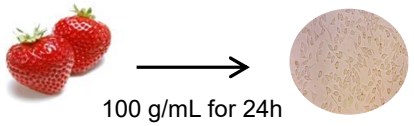
member of the statins family, used to lower cholesterol and prevent cardiovascular diseases as a consequence of the inhibition of HMG-CoA reductase.

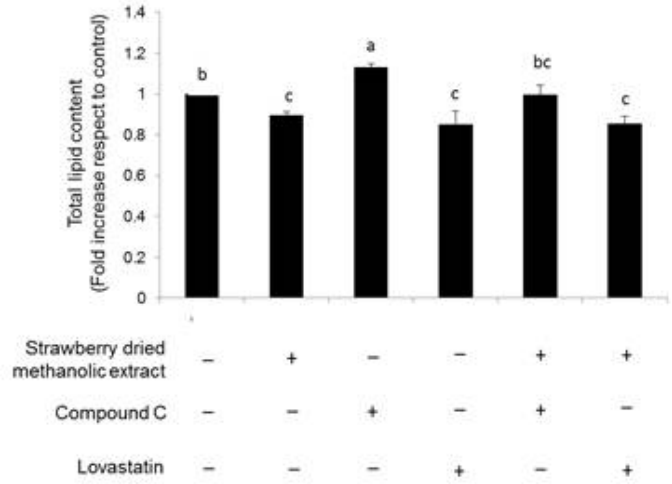


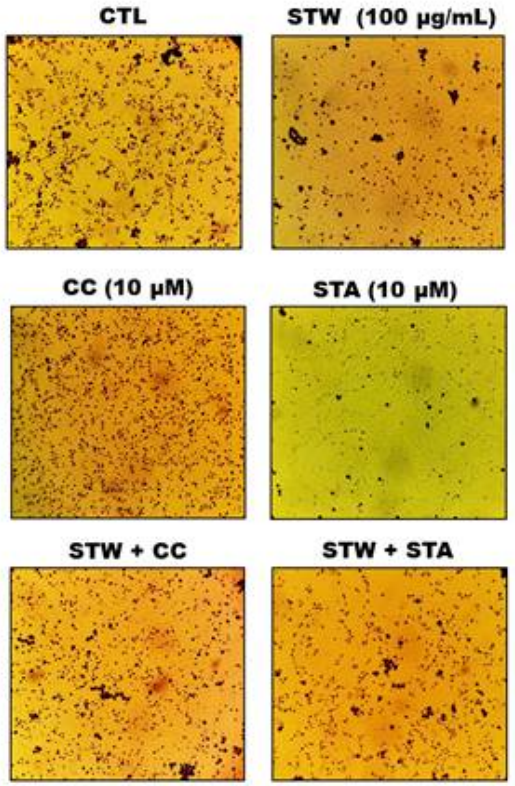
COMPOUND C ≠ STRAWBERRY = LOVASTATIN

Strawberry treatment has similar effects to the treatment with lovastatin and contrary to the obtained with Compound C regarding to lipid metabolism

Lipid-lowering properties of strawberry polyphenols







Forbes-Hernandez et al., 2017 , Nutrients, 9,621.

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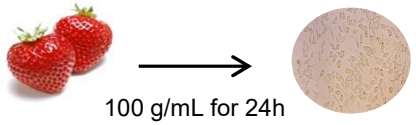

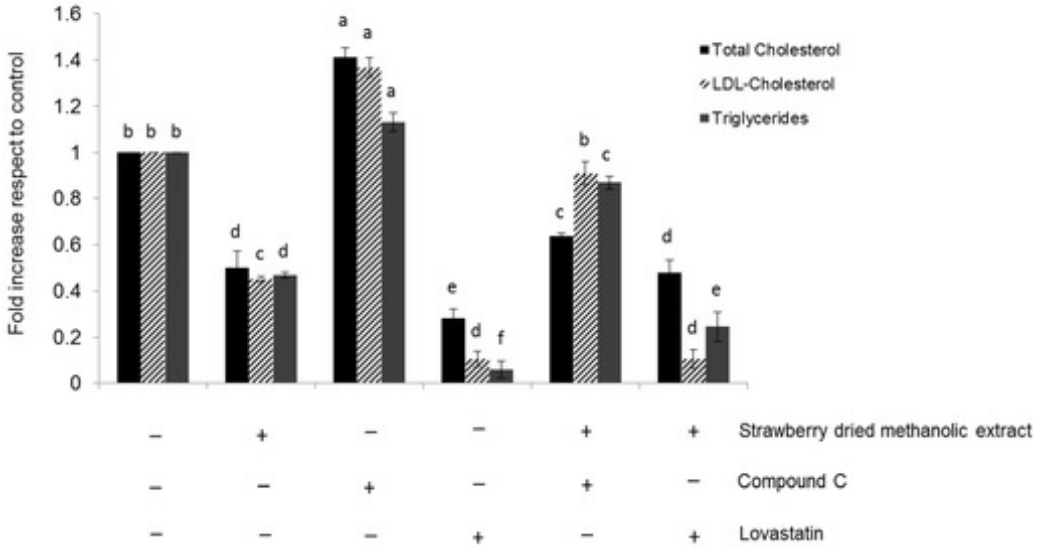

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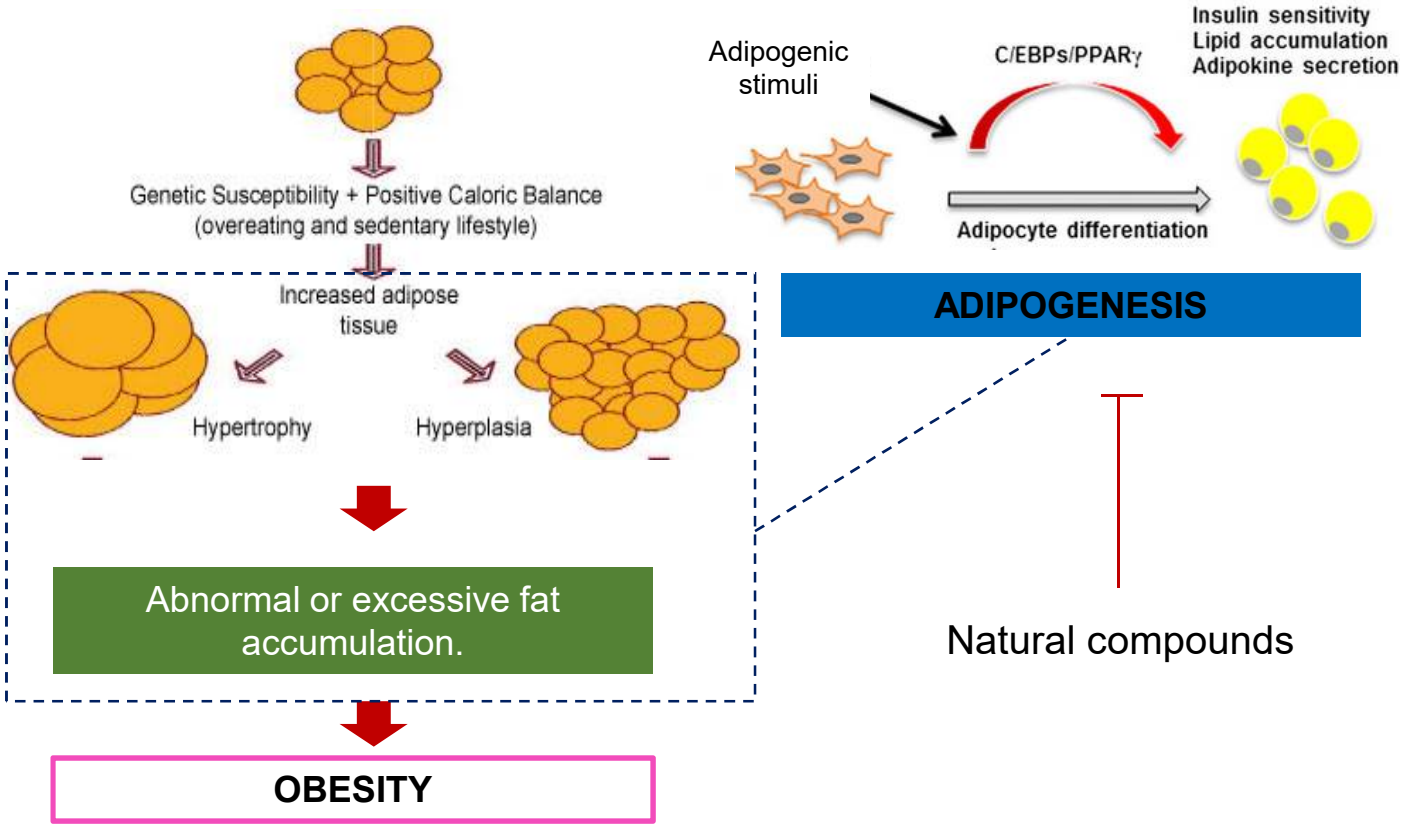


OPEN ACCESS Freely available online PLoS one

Inhibition of Adipogenesis and Induction of Apoptosis and Lipolysis by Stem Bromelain in 3T3-L1 Adipocytes

Sandeep Dave, Naval Jit Kaur, Ravikanth Nanduri, H. Kitdorlang Dkhar, Ashwani Kumar, Pawan Gupta*

OPEN ACCESS Freely available online PLoS one

α-Mangostin Induces Apoptosis and Suppresses Differentiation of 3T3-L1 Cells via Inhibiting Fatty Acid Synthase

Xiaofang Quan[1], Yi Wang[1], Xiaofeng Ma[1]*, Yan Liang[1], Weixi Tian[1], Qingyun Ma[2], Hezhong Jiang[3], Youxing Zhao[2]*

PLOS | ONE

Ursolic Acid Inhibits Adipogenesis in 3T3-L1 Adipocytes through LKB1/AMPK Pathway

Yonghan He, Ying Li, Tiantian Zhao, Yanwen Wang , Changhao Sun

JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

Article

pubs.acs.org/JAFC

Antiadipogenic Effect of Dietary Apigenin through Activation of AMPK in 3T3-L1 Cells

Mafuyu Ono and Ko Fujimori*

Research Article

Antiobesity Effects of Unripe *Rubus coreanus* Miquel and Its Constituents: An *In Vitro* and *In Vivo* Characterization of the Underlying Mechanism

Dool-Ri Oh,[1,2] Yujin Kim,[1] Eun-jin Choi,[1] Hunmi-Lee,[1] Myung-A Jung,[1] Donghyuck Bae,[1] Ara Jo,[1] Young Ran Kim,[2] and Sunoh Kim[1]

JOURNAL OF MEDICINAL FOOD
J Med Food 11 (4) 2008, 773–783

DOI: 10.1089/jmf.2008.0077

Combined Effects of Genistein, Quercetin, and Resveratrol in Human and 3T3-L1 Adipocytes

Hea Jin Park,[1] Jeong-Yeh Yang,[1] Suresh Ambati,[1] Mary Anne Della-Fera,[1] Dorothy B. Hausman,[2] Srujana Rayalam,[1] and Clifton A. Baile[1,2]

Food Chemistry 136 (2013) 1086–1094

Contents lists available at SciVerse ScienceDirect

Food Chemistry

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

Reduction of lipid accumulation in white adipose tissues by *Cassia tora* (Leguminosae) seed extract is associated with AMPK activation

Thing-Fong Tzeng[a,1], Hung-Jen Lu[b], Shorong-Shii Liou[c], Chia Ju Chang[d], I-Min Liu[c,*]

PHARMACEUTICAL BIOLOGY, 2017
VOL. 55, NO. 1, 2026–2034
https://doi.org/10.1080/13880209.2017.1345952

Taylor & Francis
Taylor & Francis Group

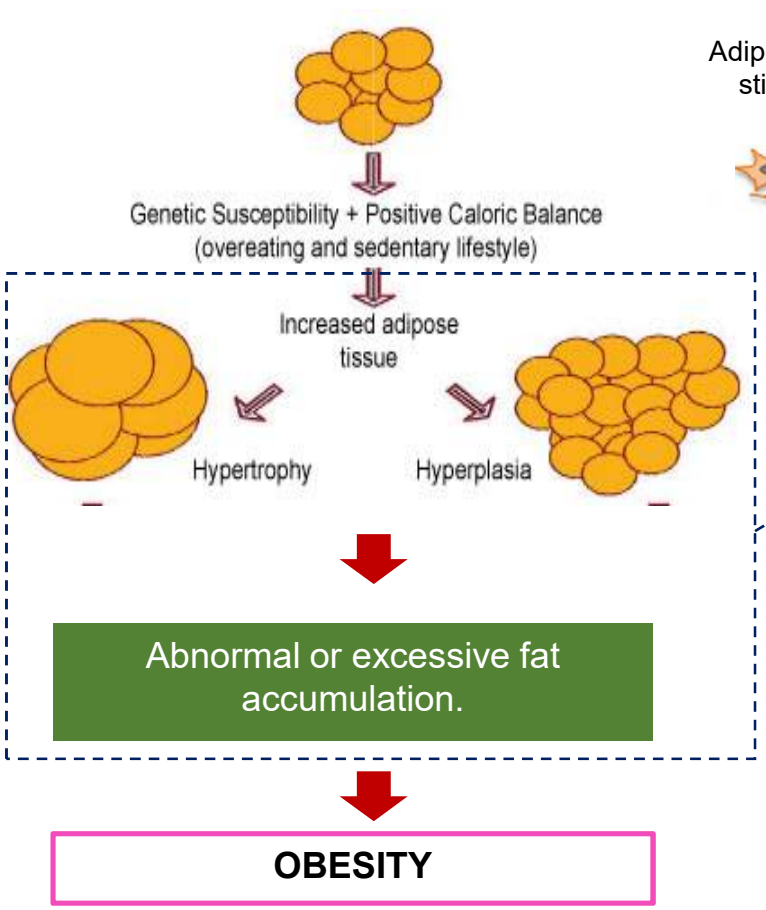
RESEARCH ARTICLE

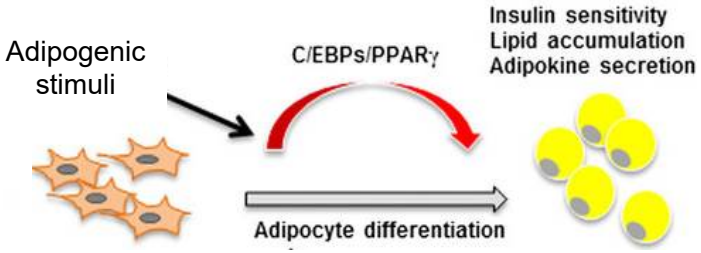
OPEN ACCESS Check for updates

Caffeic acid methyl and ethyl esters exert potential antidiabetic effects on glucose and lipid metabolism in cultured murine insulin-sensitive cells through mechanisms implicating activation of AMPK

Hoda M. Eid[a,b,c], Farah Thong[d], Abir Nachar[a,b] and Pierre S. Haddad[a,b]

HOW CAN OBESITY BE DEFINED?

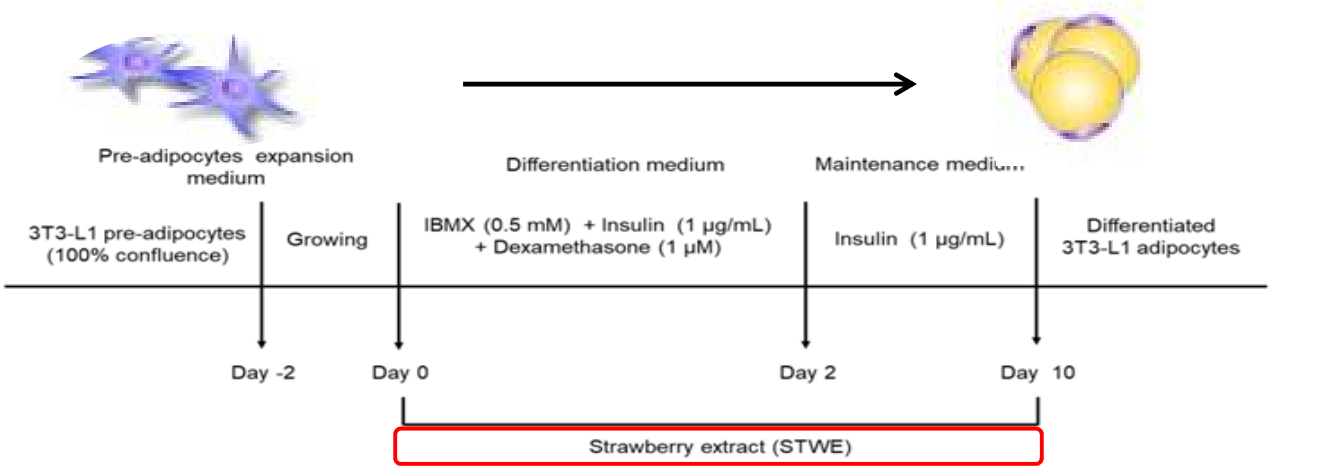


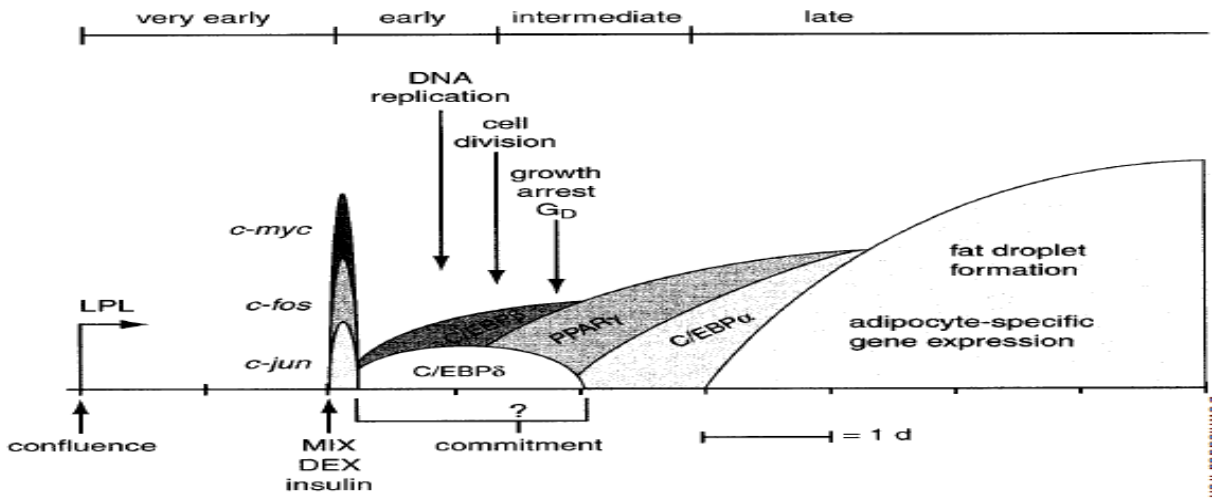


ADIPOGENESIS

Could strawberries bioactive compounds regulate adipogenesis?

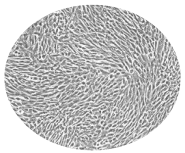
PROGRESSION OF 3T3-L1 PREADIPOCYTE DIFFERENTIATION

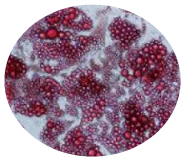




EXPERIMENTAL DESIGN

Pre-adipocytes





Mature adipocytes

Evaluation of cell functions:

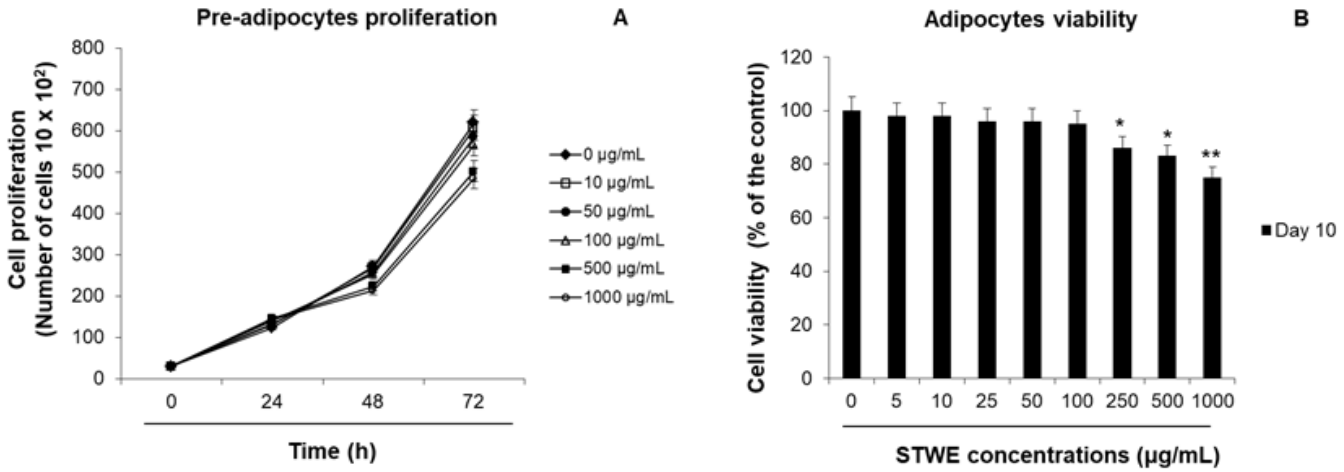
- Viability assay
- Apoptosis
- Intracellular ROS production
- Antioxidant enzymes activities
- Mitochondrial functionality

Lipid metabolism:

- LDL-cholesterol and TAGs contents
- Lipid peroxidation
- Total lipid accumulation

Adipogenic gene and protein expressions

EFFECTS OF STRAWBERRY EXTRACT (STWE) ON PROLIFERATION AND VIABILITY OF 3T3-L1 CELLS



No significant (toxic) effect on cell proliferation was observed at concentrations of STWE ≤100 µg/mL

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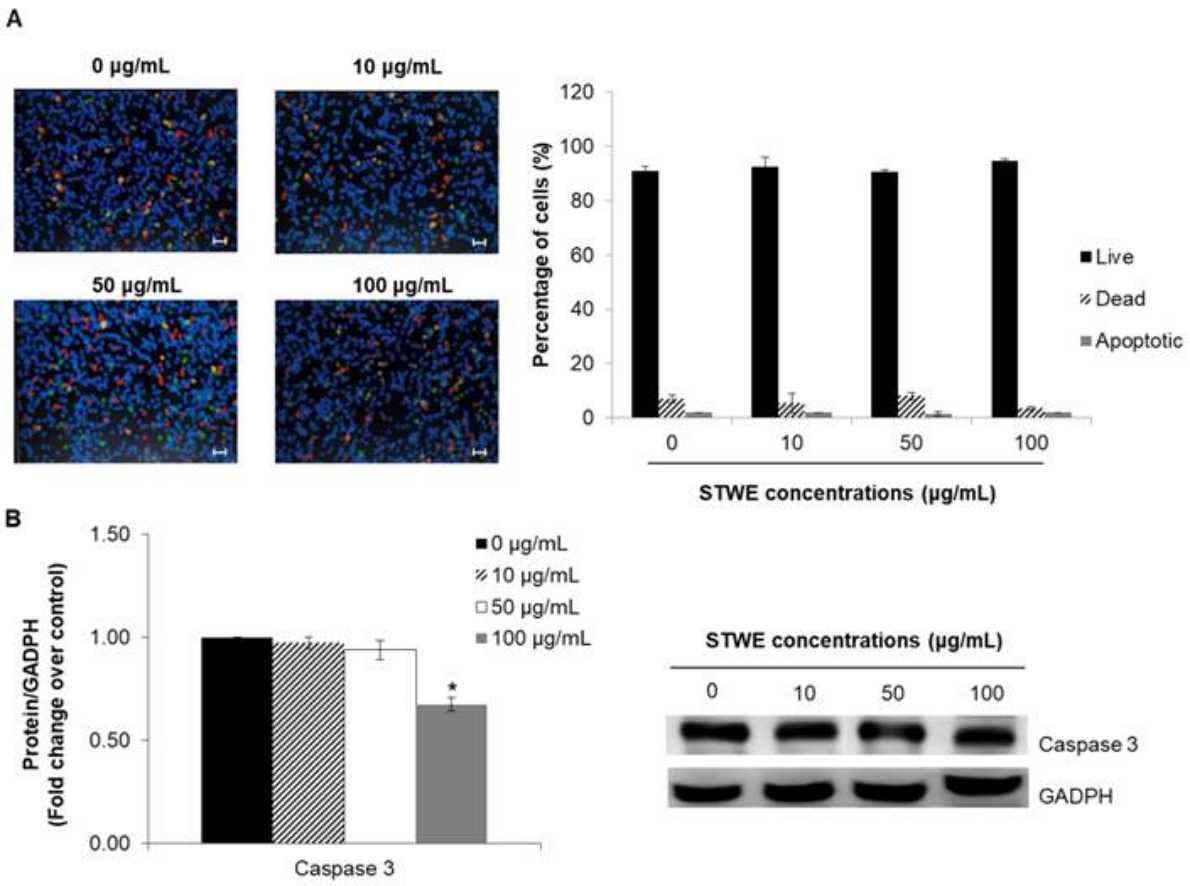
EFFECTS OF STWE ON MATURE ADIPOCYTES APOPTOSIS



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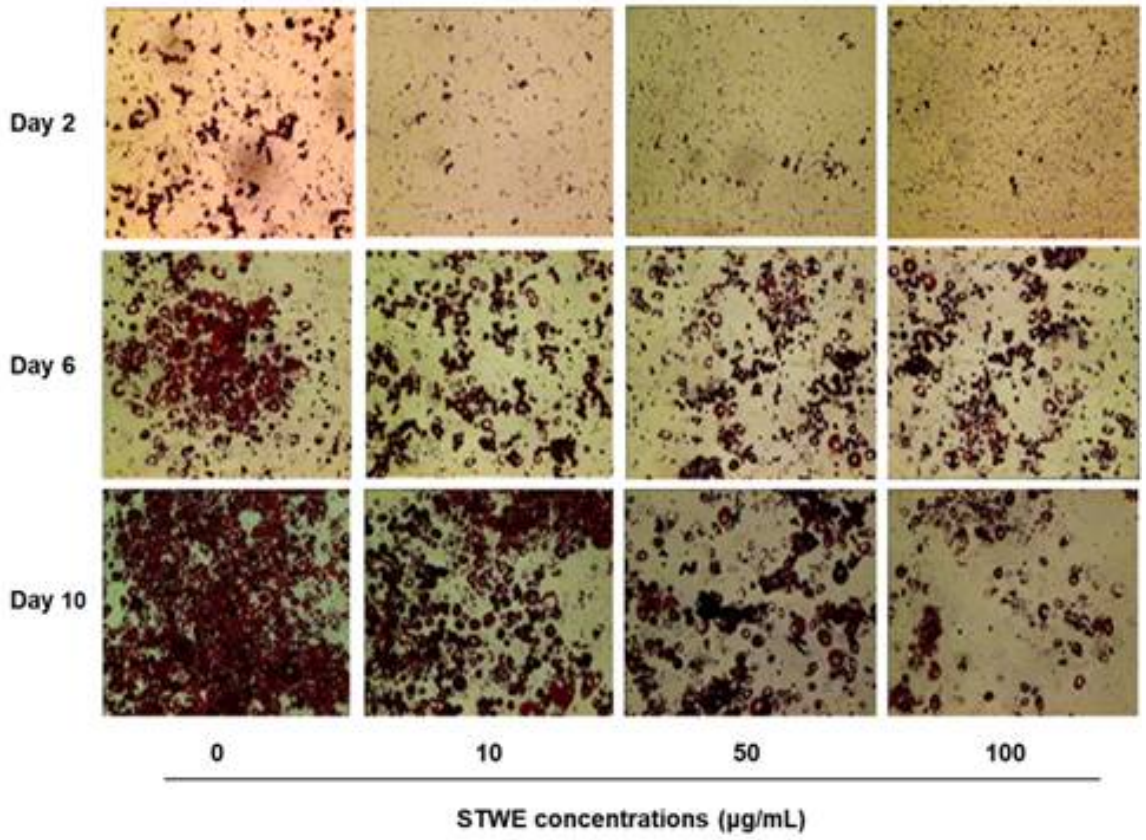
EFFECTS OF STWE ON 3T3-L1 CELLS DIFFERENTIATION



Inhibition of adipogenesis

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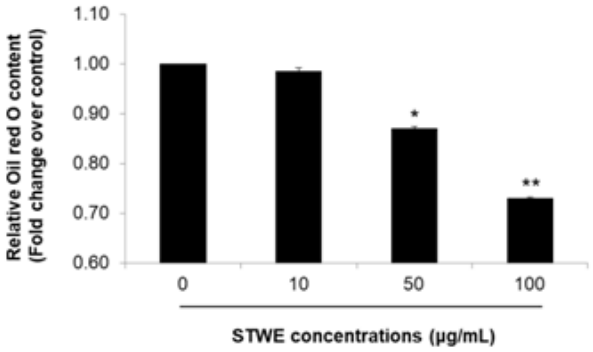
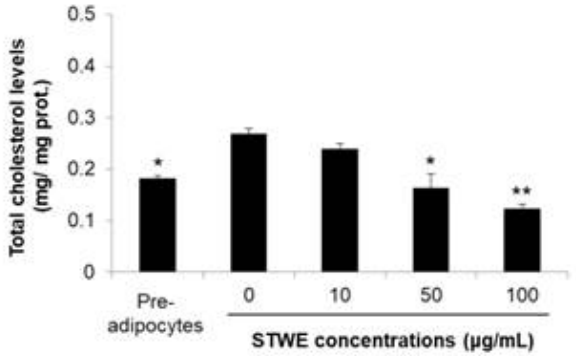
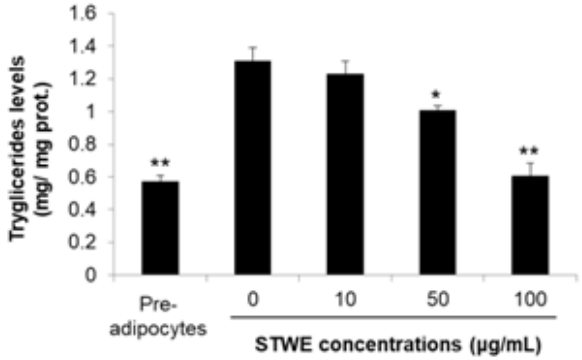
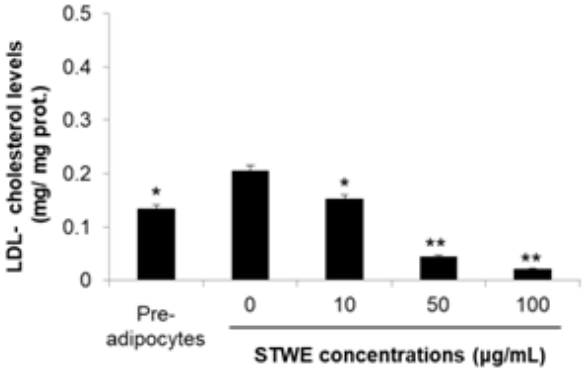
EFFECTS OF STWE ON LIPID ACCUMULATION





Decrease of total lipid content and improvement of lipid profile





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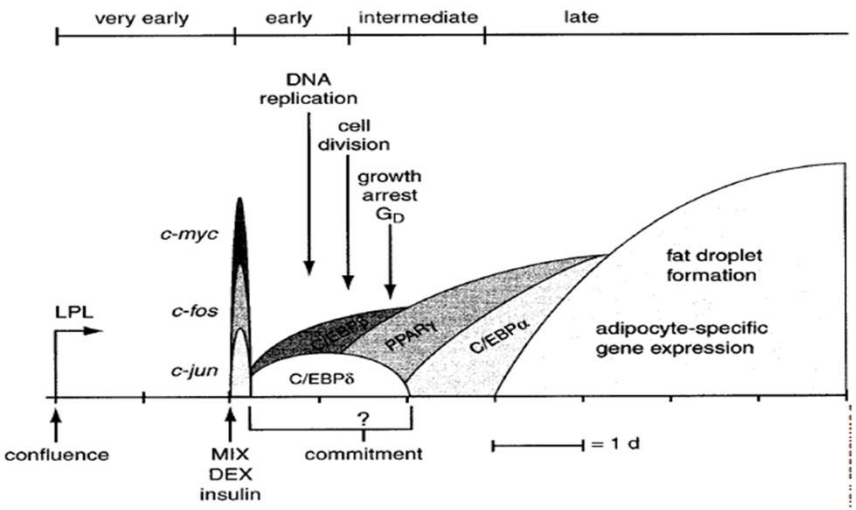
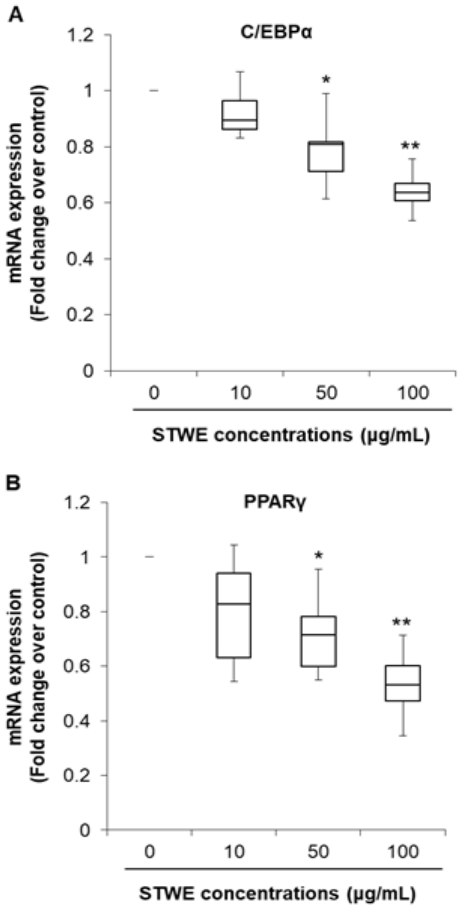
EFFECTS OF STWE ON THE ADIPOGENIC TRANSCRIPTION FACTORS

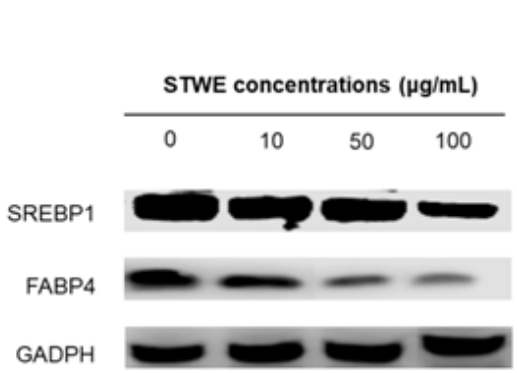


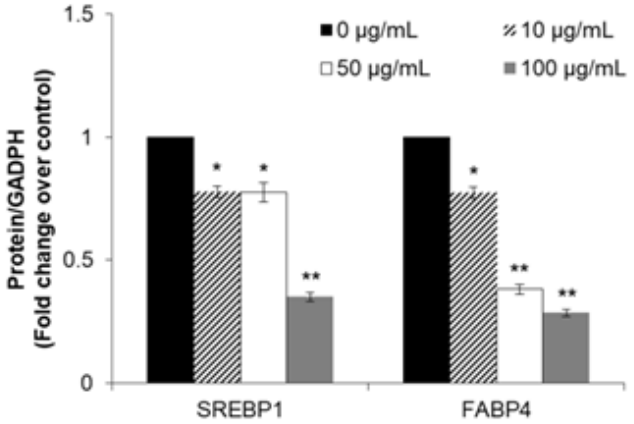


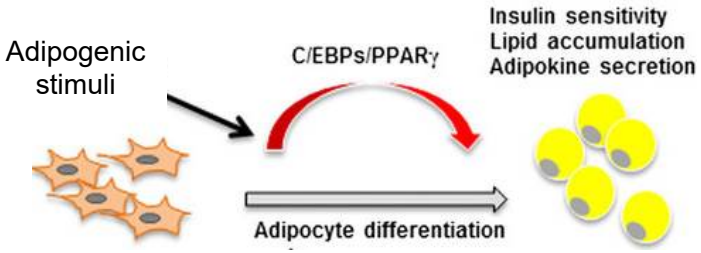
Decrease of mRNA expression of C/EBP-α and PPAR-γ

Forbes-Hernandez et al., Food Funct., 2020,11, 297-304

EFFECTS OF STWE ON THE DIFFERENTIATION RELATED TRANSCRIPTION FACTORS







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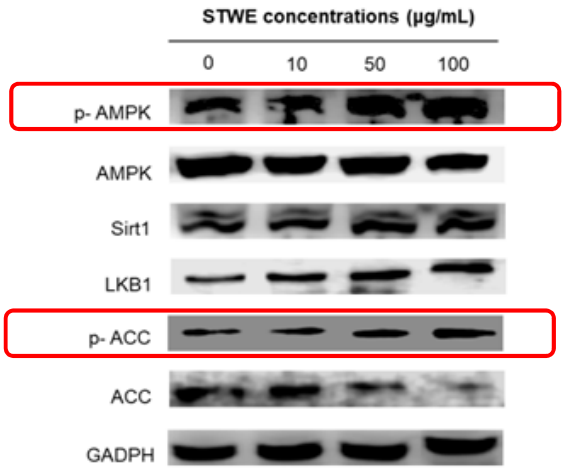
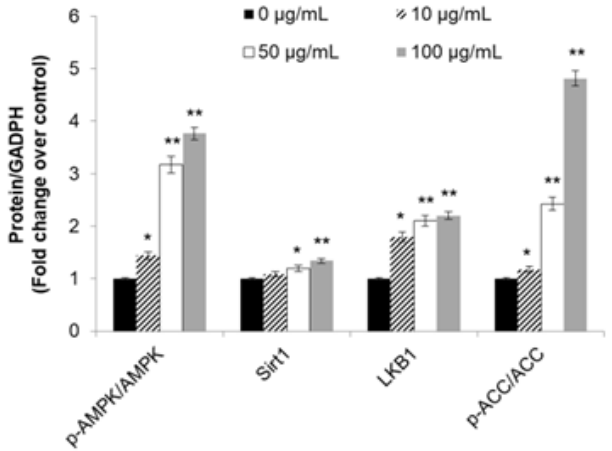
EFFECTS OF STWE ON THE DIFFERENTIATION RELATED TRANSCRIPTION FACTORS





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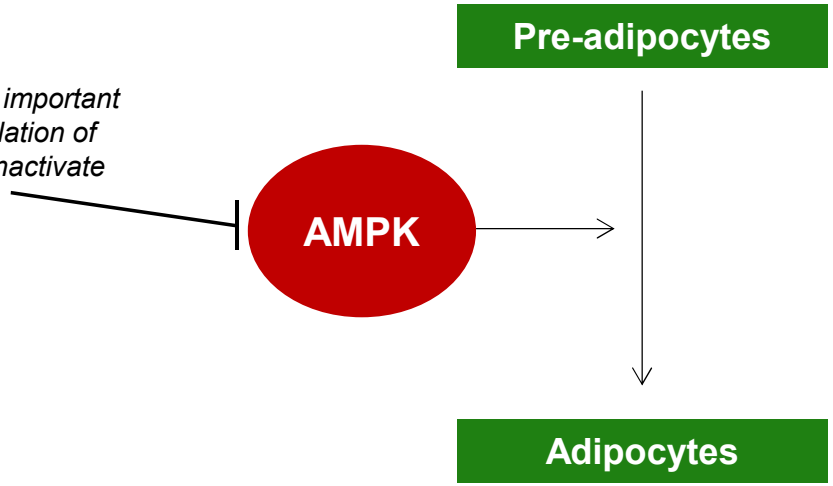
How to confirm the involvement of AMPK pathway in the strawberry mechanisms of action?

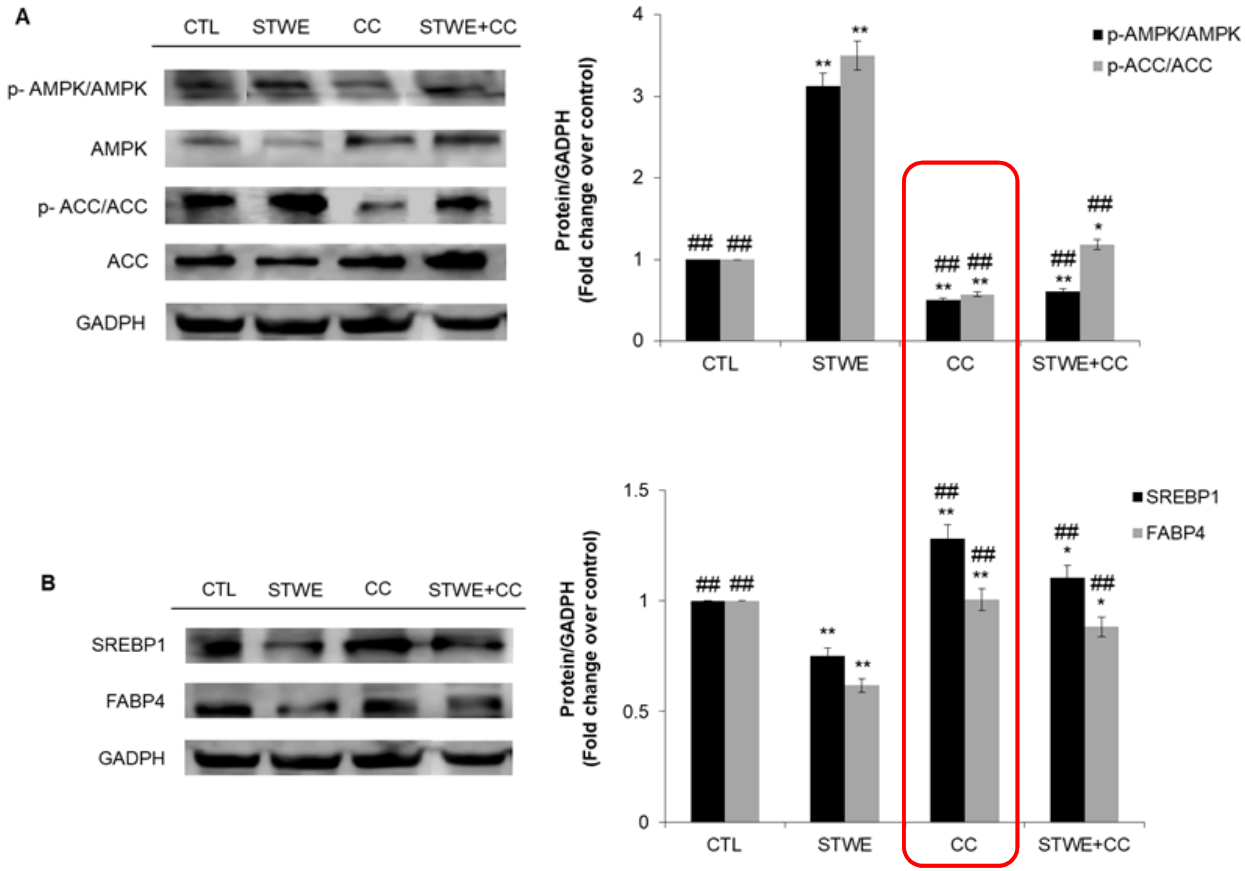
COMPOUND C

pharmacological compound with the important function of blocking the phosphorylation of AMPK and, as a consequence, to inactivate this protein.



COMPOUND C ≠ STRAWBERRY

EFFECTS OF AMPK INHIBITION IN THE EXPRESSION OF LIPOGENESIS AND FATTY ACIDS OXIDATION RELATED PROTEINS



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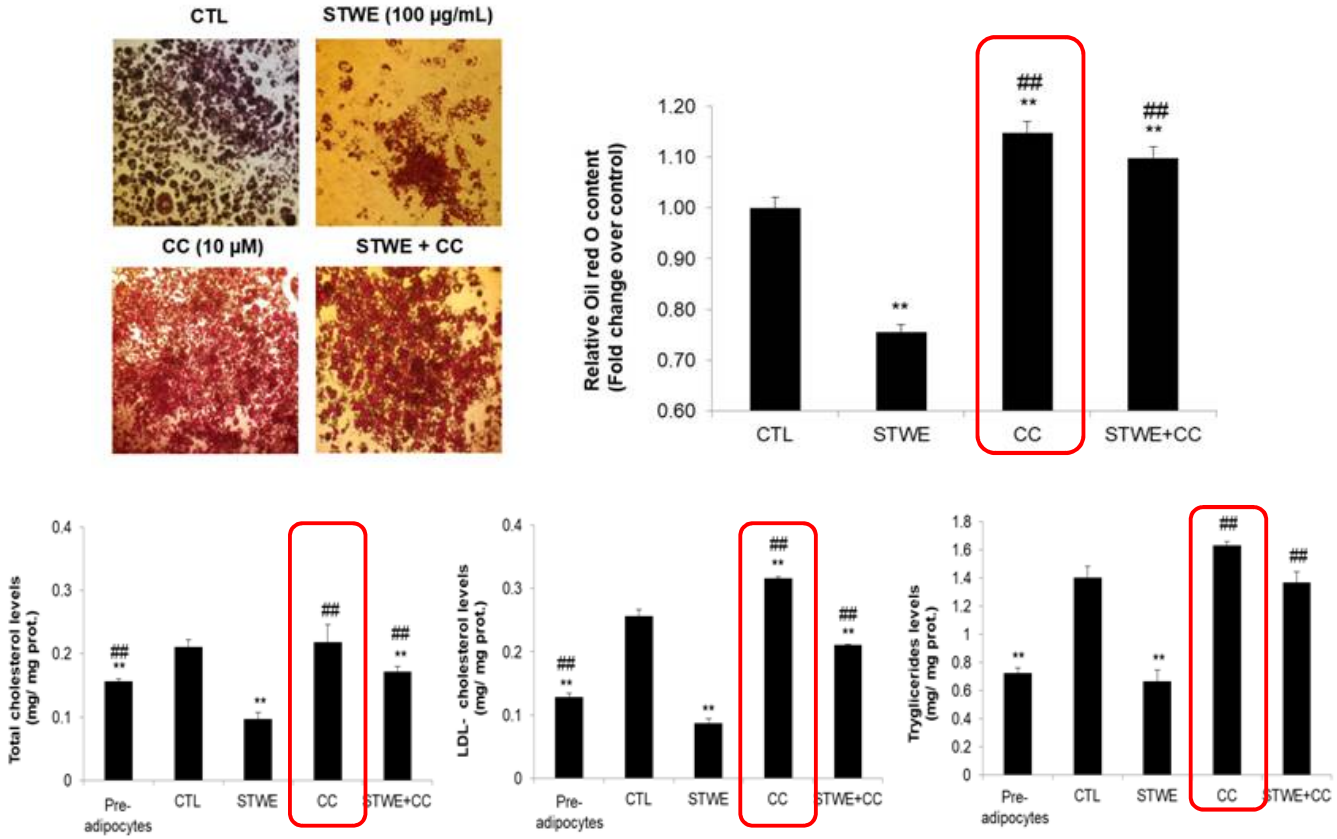
EFFECTS OF AMPK INHIBITION ON THE EXPRESSION OF LIPOGENESIS AND LIPID PROFILE



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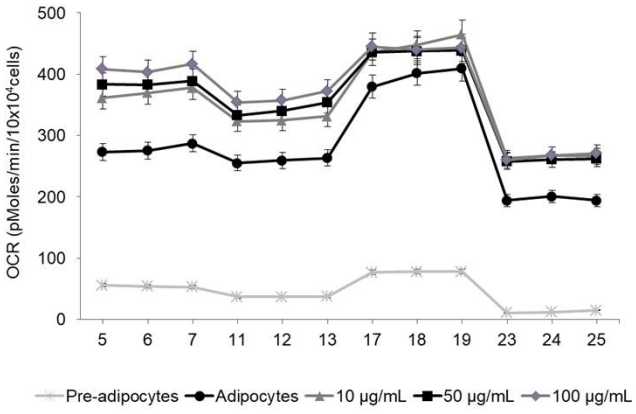
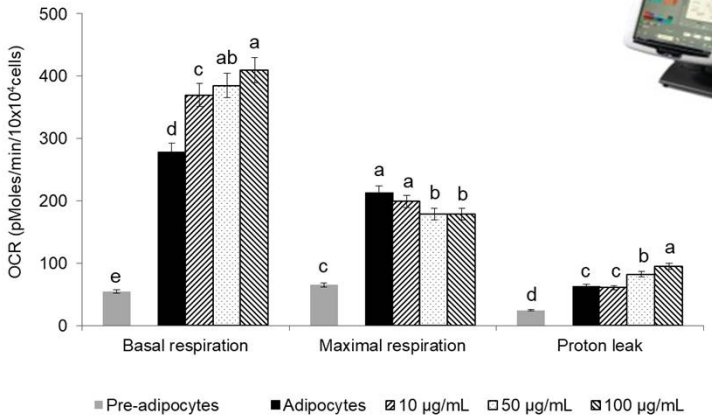
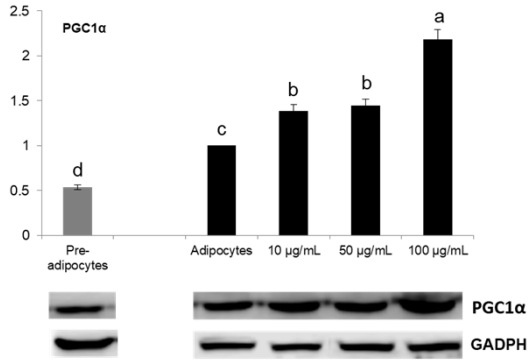
EFFECTS OF STWE ON CELLULAR METABOLISM







Mitochondrial Respiration

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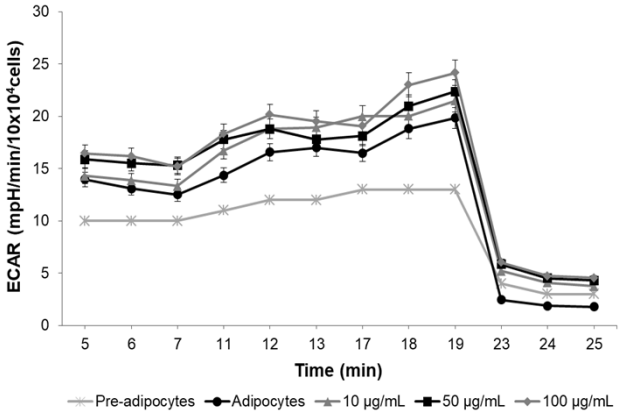
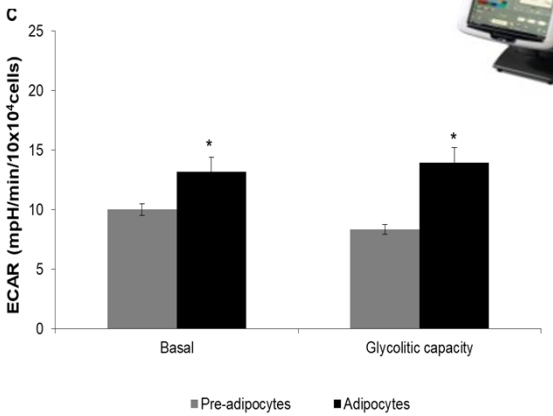
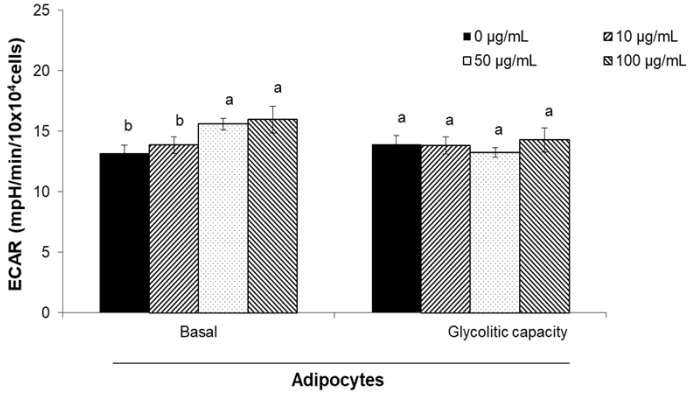
EFFECTS OF STWE ON CELLULAR METABOLISM







Glycolytic function

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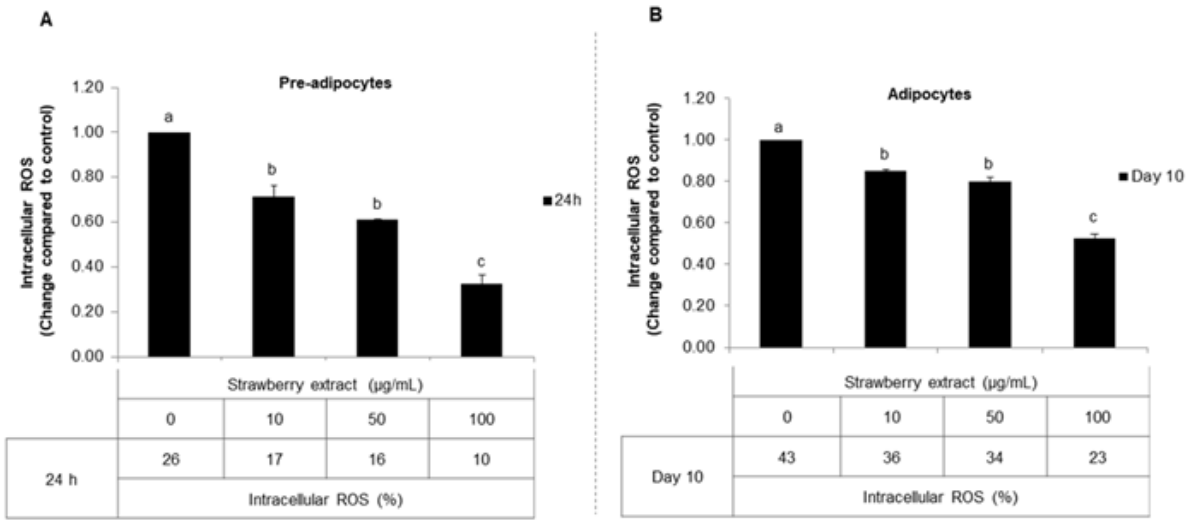
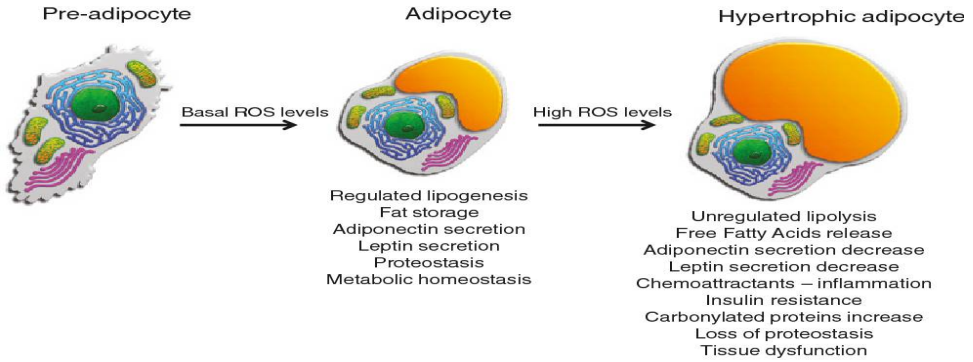
EFFECTS OF STWE ON INTRACELLULAR ROS PRODUCTION





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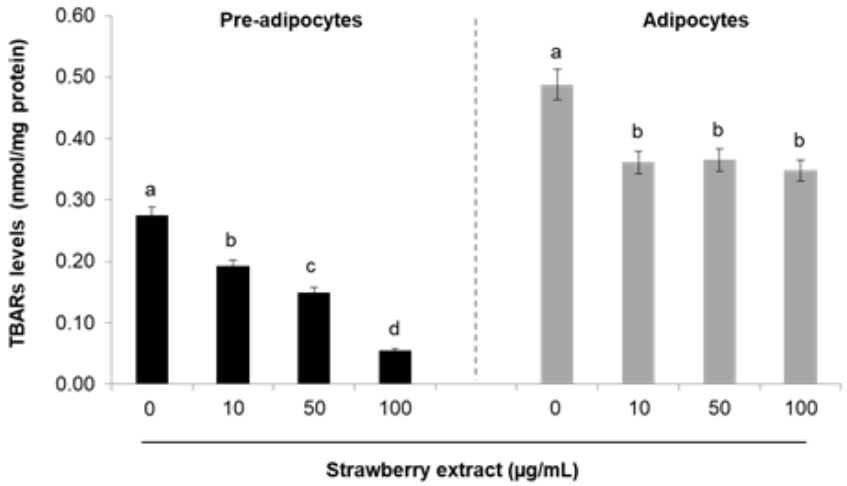
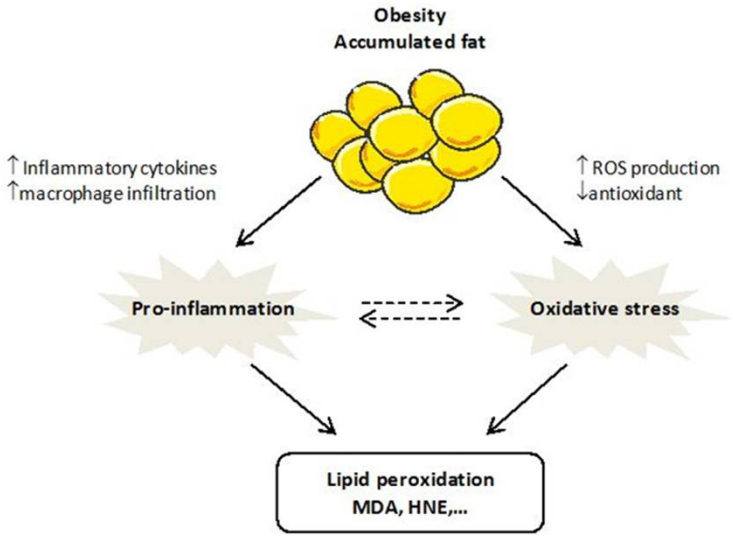
EFFECTS OF STWE ON LIPID PEROXIDATION





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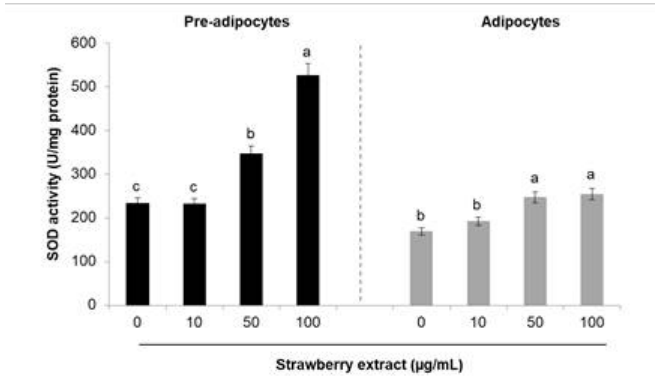
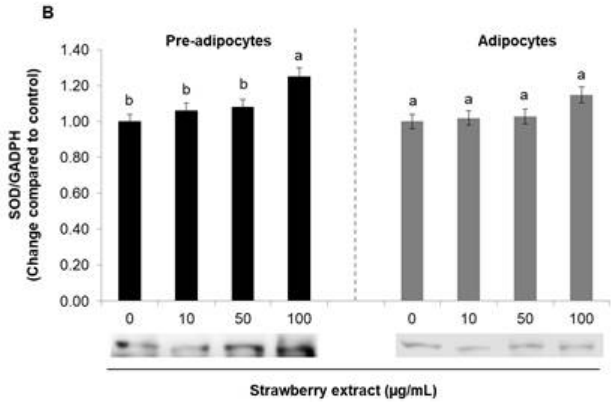
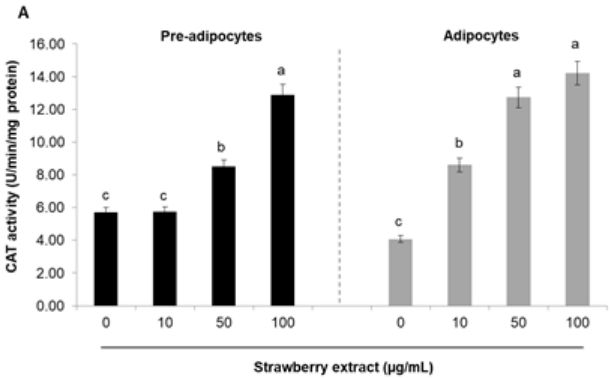
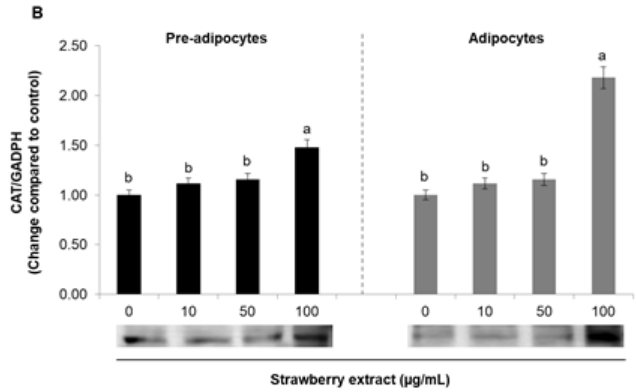
EFFECTS OF STWE ON ANTIOXIDANT ENZYMES ACTIVITY AND PROTEIN EXPRESSION









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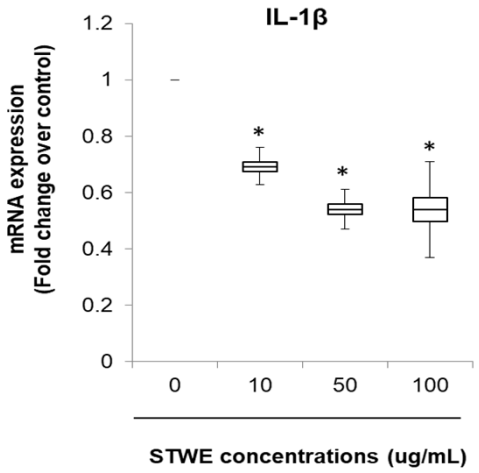
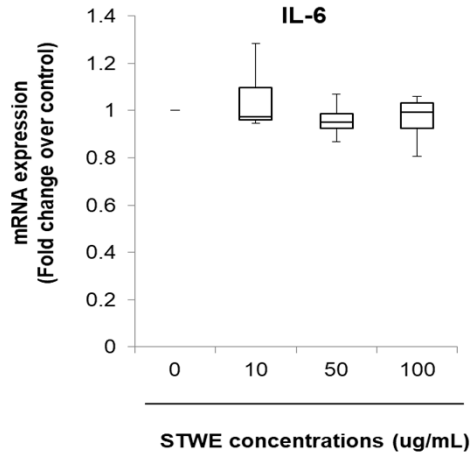
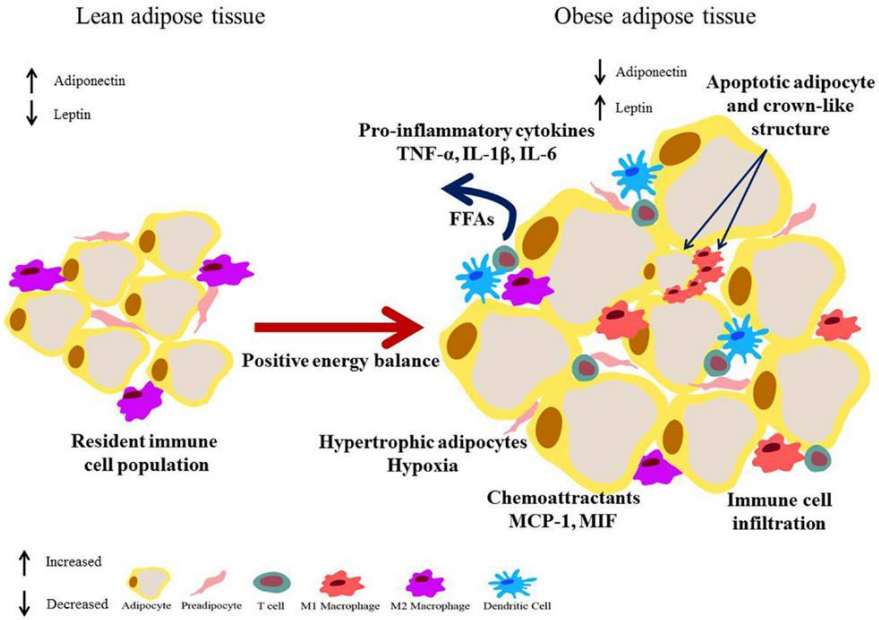
EFFECTS OF STWE ON LIPID PRO-INFLAMMATORY CYTOKINES







https://doi.org/10.3389/fendo.2013.00052

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The Journal of Nutritional Biochemistry
Volume 25, Issue 3, March 2014, Pages 289–294

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

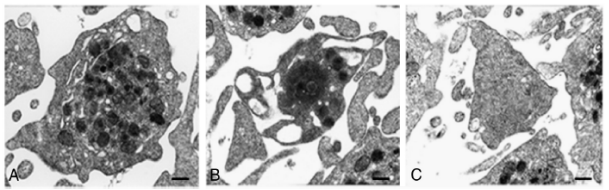
José M. Alvarez-Suarez[a], Francesca Giampieri[a, b], Sara Tulipani[c], Tiziana Casoli[d], Giuseppina Di Stefano[e], Ana M. González-Paramás[f], Celestino Santos-Buelga[f], Franco Busco[g], Josè L. Quiles[h], Mario D. Cordero[i], Stefano Bompadre[j], Bruno Mezzetti[b], Maurizio Battino[a,]

23 healthy volunteers

Ingestion of 500 g of strawberries

Strawberries consumption improves plasma lipids profile, biomarkers of antioxidant status, antihemolytic defenses and platelet function in healthy subjects.

Parameters (reference values)	Baseline	Time 30d	Washout
General biochemical analysis			
Total cholesterol (mmol/L)	4.58±0.13[a]	4.18±0.12[b]	4.50±0.12[a]
HDL-C (mmol/L)	1.54±0.07[a]	1.57±0.07[a]	1.52±0.06[a]
LDL-C (mmol/L)	2.54±0.10[a]	2.19±0.09[b]	2.52±0.10[a]
Triglycerides (mmol/L)	0.85±0.09[a]	0.67±0.06[b]	0.82±0.06[a]



Resting state

Central clustered platelet, activation phase

Degranulated platelet, end of activation process

Home messages...

- STWE significantly reduced 3T3-L1 pre-adipocytes differentiation and lipid accumulation via the AMPK signaling pathway providing new insights into the molecular mechanism by which this STWE suppresses adipogenesis.

- STWE supplementation significantly decreased ROS production and lipid peroxidation while increased antioxidant enzymes activities and expression in both pre-adipocytes and matures adipocytes.

It would be interesting to investigate whether strawberry extracts are equally efficient at all stages of differentiation or otherwise in one or more of them.

STWE could be a promising naturally occurring therapeutic agent for the prevention and treatment of obesity.

Thank you for your kind attention