

TAVOLA ROTONDA

Moderatori:

Michela Barichella, Gianni Pezzoli

11 MAGGIO 2018

**Nanotechnology-based
polyphenol delivery systems
for the treatment of
Neurodegenerative and
Neuro-Oncology diseases**



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Proposed biological processes triggered by dietary polyphenols

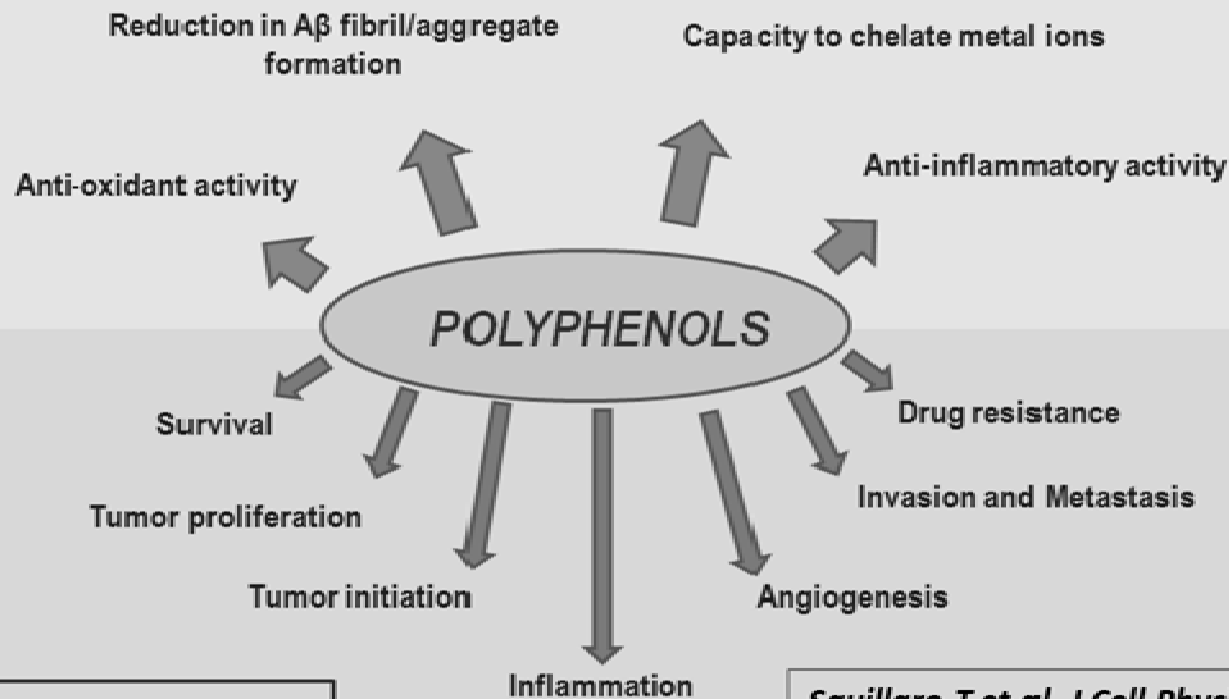
Journal of Cellular Physiology

REVIEW ARTICLE | Full Access

Adult-onset brain tumors and neurodegeneration: Are polyphenols protective?

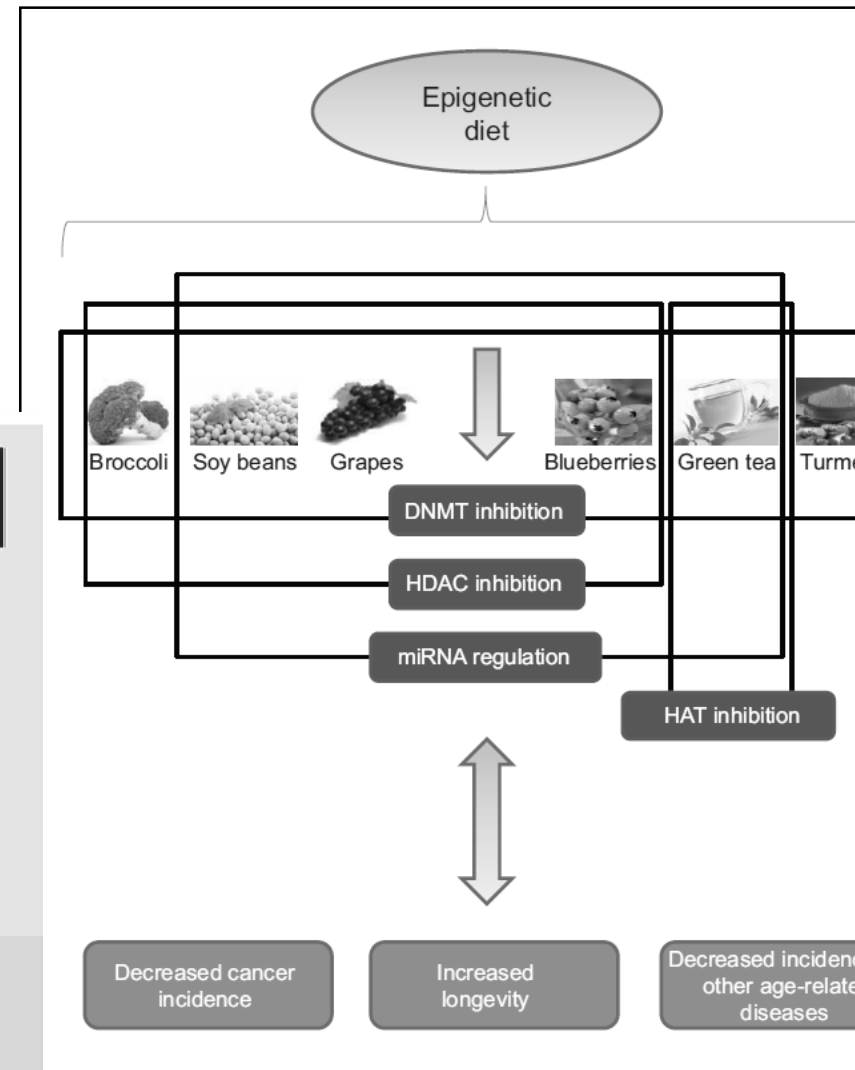
Tiziana Squillaro, Carla Schettino, Simone Sampaolo, Umberto Galderisi, Giuseppe Di Iorio, Antonio Giordano, Mariarosa A. B. Melone

NEURODEGENERATIVE DISORDERS
Prevention and Treatment



BRAIN TUMORS
Prevention and Treatment

Squillaro T et al. J Cell Physiol
2018 May; 233(5):3955-3967



DNA methyltransferase (DNMT) inhibition
Histone deacetylase inhibition (HDAC inhibition)
Histone acetyltransferase (HAT) inhibition
MicroRNAs (miRNAs) regulation

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...our results



RESEARCH ARTICLE

Published: March 18, 2015

Ruta graveolens L. Induces Death of Glioblastoma Cells and Neural Progenitors, but Not of Neurons, via ERK 1/2 and AKT Activation

Maria Teresa Gentile¹, Claudia Ciniglia¹✉, Mafalda G. Reccia¹✉, Floriana Volpicelli^{2,3}, Monica Gatti⁴, Stefano Thellung⁴, Tullio Florio⁴, Mariarosa A. B. Melone^{5,6}, Luca Colucci-D'Amato^{1,6*}



Contents lists available at ScienceDirect

Neurochemistry International

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

ine exacerbates mutant Huntingtin toxicity via oxidative-
ted inhibition of autophagy in SH-SY5Y neuroblastoma cells:
cial effects of anti-oxidant therapeutics

Vidoni^a, Andrea Castiglioni^a, Christian Seca^a, Eleonora Secomandi^a,
sa A.B. Melone^{b, c, **}, Ciro Isidoro^{a, c, *}

Neurochem Int. 2016 Dec;101:132-143.



nutrients



Synergistic Interplay between Curcumin and Polyphenol-Rich Foods in the Mediterranean Diet: Therapeutic Prospects for Neurofibromatosis 1 Patients

Teresa Esposito¹, Carla Schettino², Paola Polverino², Salvatore Allocca¹, Laura Adelfi¹,
Alessandra D'Amico³, Guglielmo Capaldo², Bruno Varriale⁴, Anna Di Salle⁵ ,
Gianfranco Peluso⁵, Giuseppe Sorrentino⁶, Giacomo Lus², Simone Sampaolo² ,
Giuseppe Di Iorio² and Mariarosa Anna Beatrice Melone^{2,*}

Published: 21 July 2017

Melone M et al., Effects of dietary therapy in patients with Parkinson's
(PD) XX World Congress on Parkinson's Disease and Related Disorders, G
8-11, December 2013

Resveratrol protects neuronal-like cells expressing mutant Hunt
from dopamine toxicity by rescuing ATG4-mediated autophago
formation

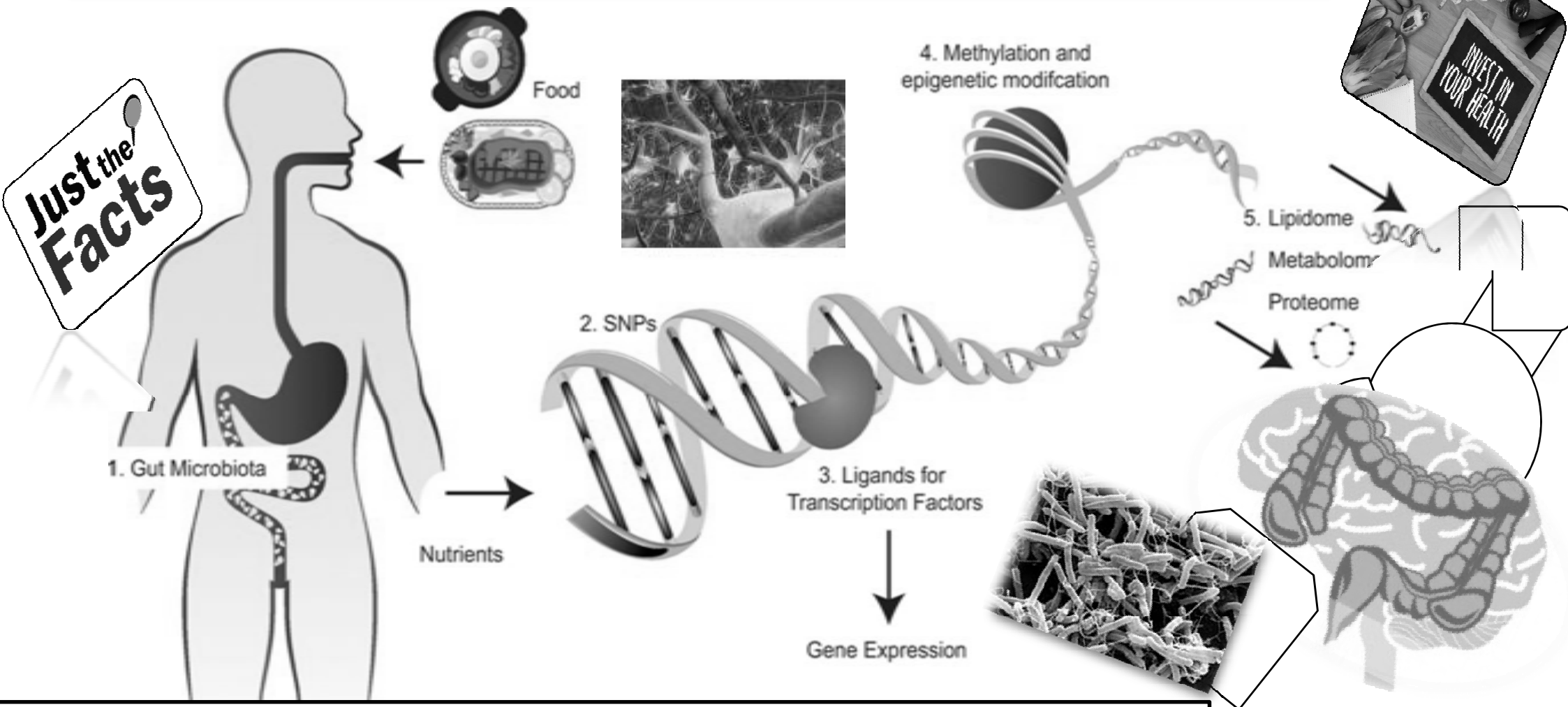
Chiara Vidoni^a, Eleonora Secomandi^a, Andrea Castiglioni^a, Mariarosa A.B. Melon
Ciro Isidoro^{a, c, *}

Neurochem Int. 2017 May 19.

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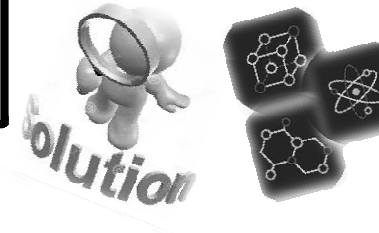


Polyphenol bioavailability: a limitation for their clinical potential



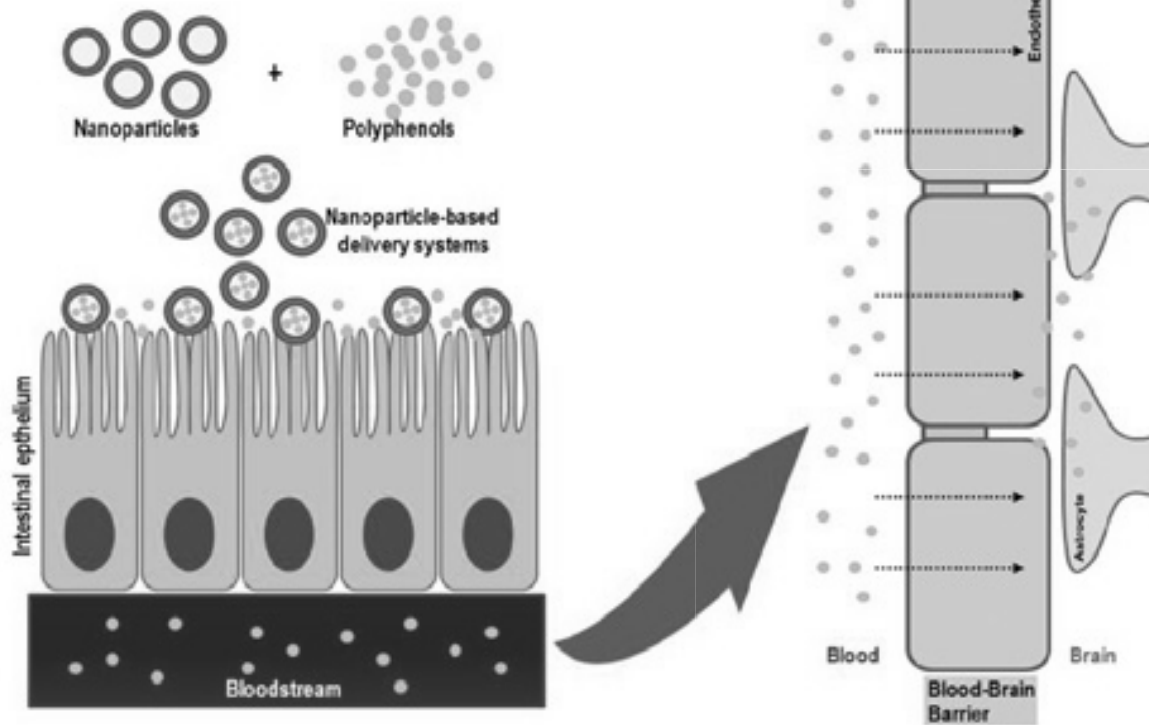
Low bioavailability of polyphenols is due to:
Intrinsic factors (chemical structure, molecular weight and low hydrosolubility);
Extrinsic factors (low stability in the gastrointestinal tract, extensive phase I and II metabolism and rapid elimination)

Nanotechnology-based delivery systems: an innovative strategy for polyphenol application in clinical practice



Polymeric nanoparticle-based delivery systems are able to encapsulate bioactive molecules in order to:

growing body literature has focused on nanotechnology-based delivery systems for improving polyphenol bioavailability



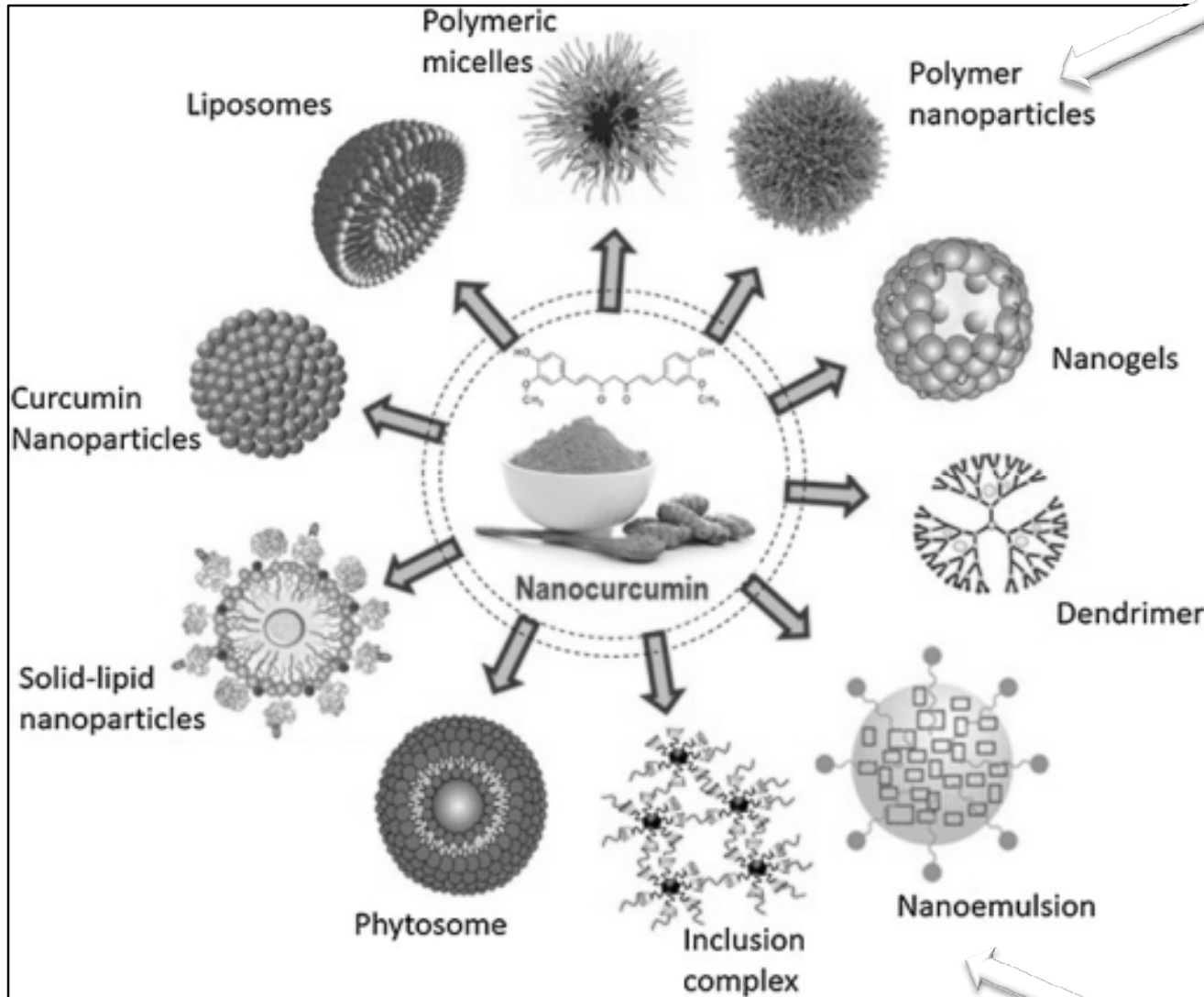
- protect them from stomach acid condition;
- ameliorate their absorption across gastrointestinal tract;
- enhance their bioavailability;
- transport them to target organs;
- improving their ability to cross the blood-brain barrier.

Squillaro T et al., Austin Aging Research Journal, 2017

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Different strategies of curcumin nanoformulation preparation

...our research



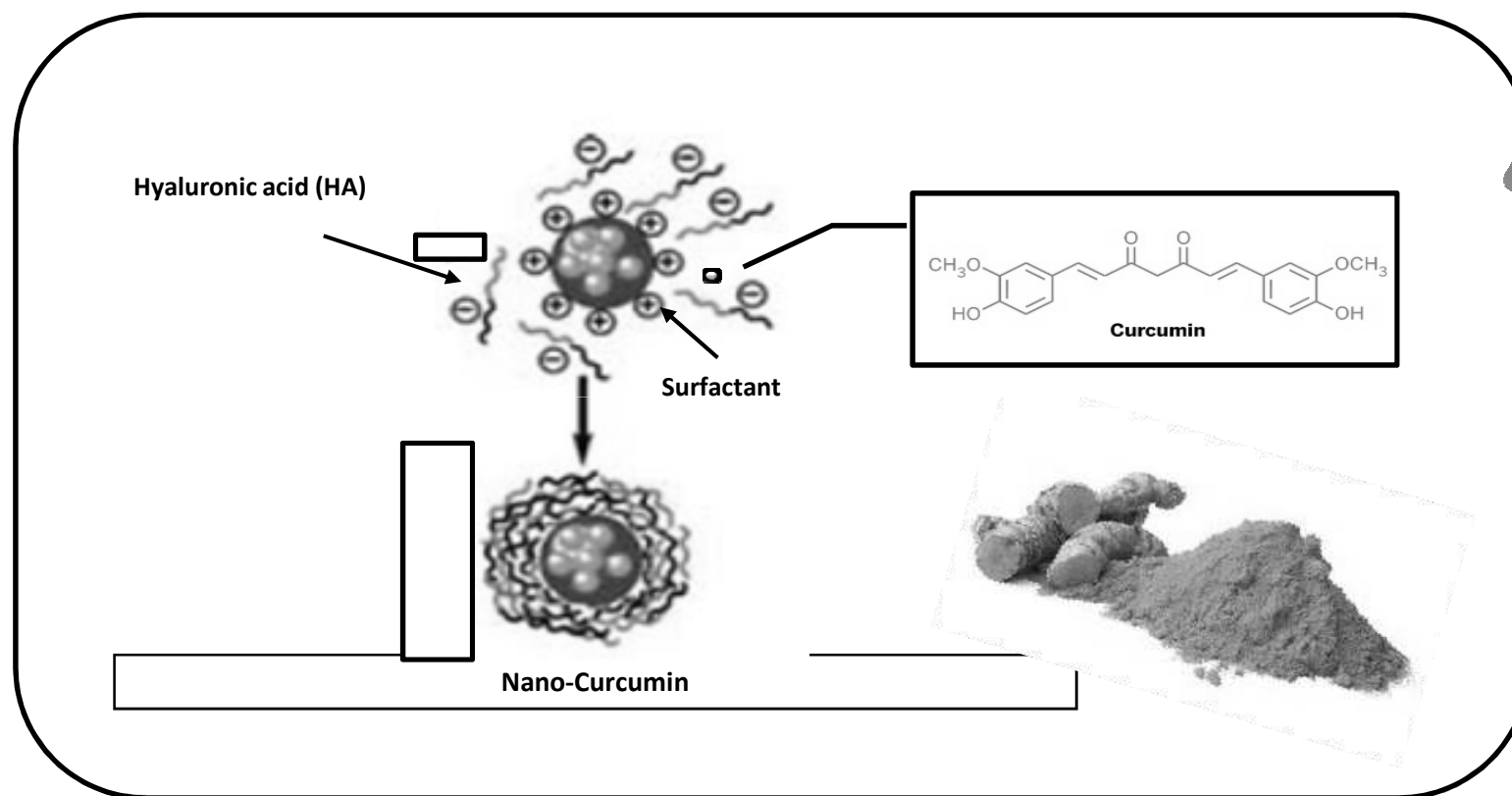
To date, several nanoparticle-based polyphenol delivery systems have been developed showing both biocompatibility and biodegradability characteristics and high efficacy regarding drug encapsulation, stability, and delivery

1. Liposomes
2. Polymeric micelles
3. Polymer nanoparticles
4. Nanogels
5. Dendrimer
6. Nanoemulsion
7. Inclusion complex
8. Phytosomes
9. Solid lipid nanoparticles
10. Curcumin nanoparticles

o T et al., Nano-delivery systems for encapsulation of dietary polyphenols:
 using tool for neurodegenerative diseases and brain tumors.
 nical Pharmacology, In press

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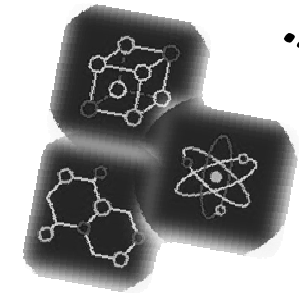
Polymeric Nanoparticles: synthesis and characterization



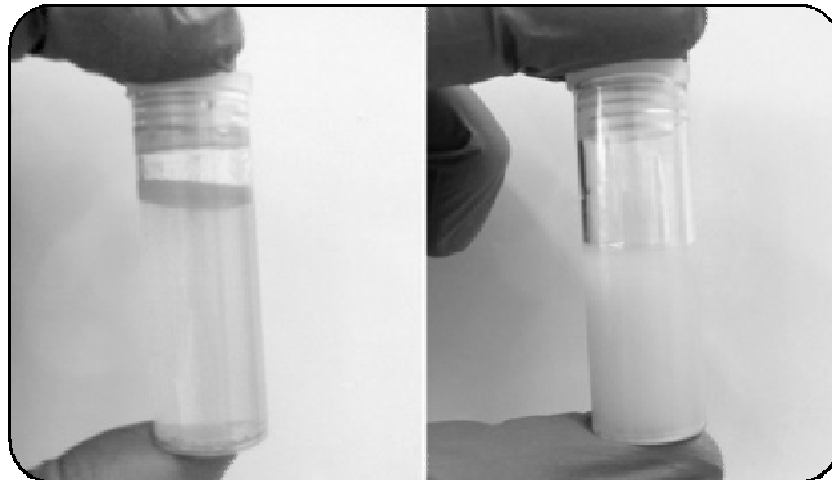
Schematic representation of nano-curcumin synthesis



Polymeric Nanoparticles: synthesis and characterization



...our results

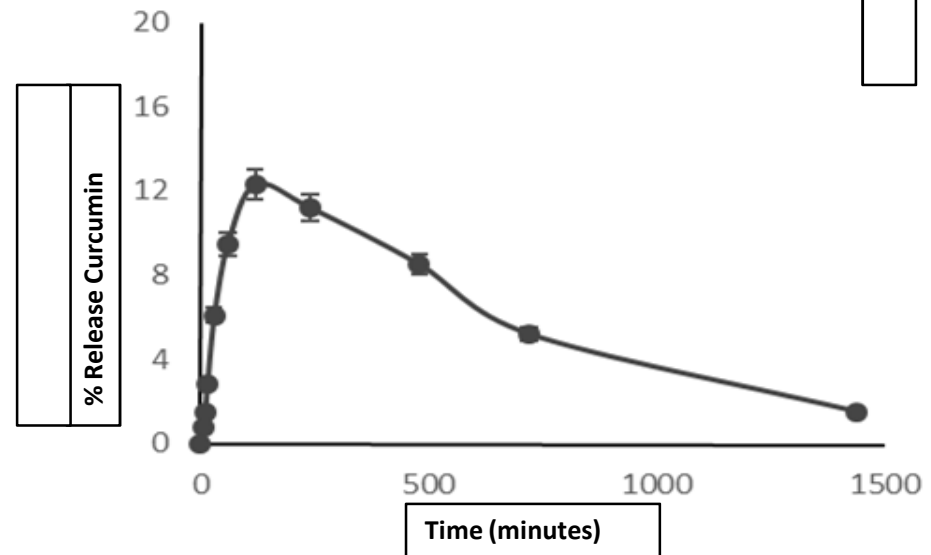


free Curcumin
in water

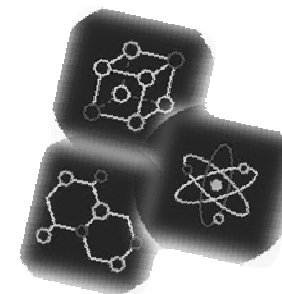
Nano-Curcumin
in water

Nano-curcumin exhibited increased water solubility compared to free curcumin.

Release kinetics of curcumin from nano-curcumin demonstrates a burst release of 60% over the first 4 hours and a subsequent release of 10% over the next 20 hours.



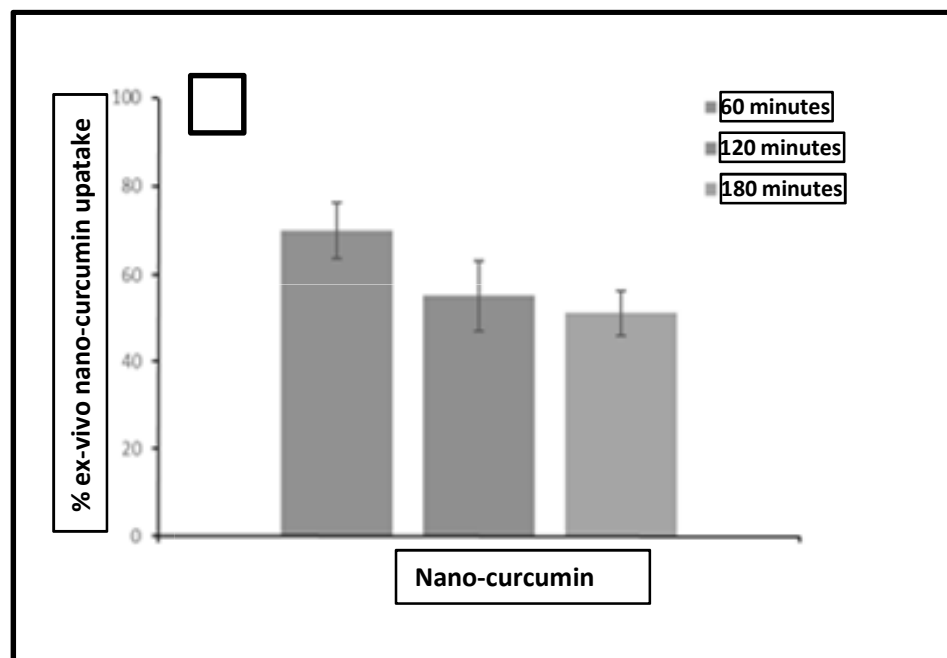
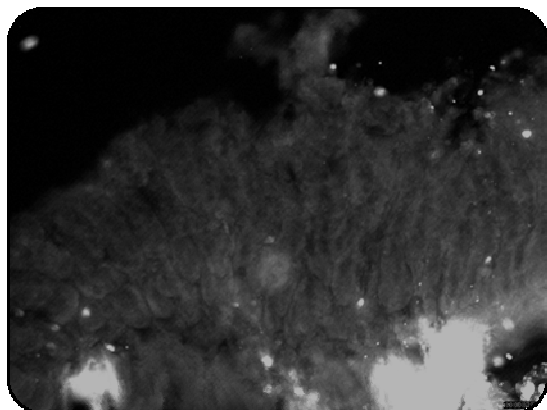
Polymeric Nanoparticles: synthesis and characterization



...our results

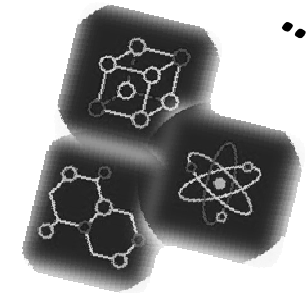
Nano-Curcumin *ex-vivo* uptake

60 minutes uptake



The **human adenocarcinoma *Caco-2* cell line** is a widely used cellular *model* to evaluate the ability of small molecules such as curcumin to **cross the intestinal barrier**, as well as to study their transport mechanisms.

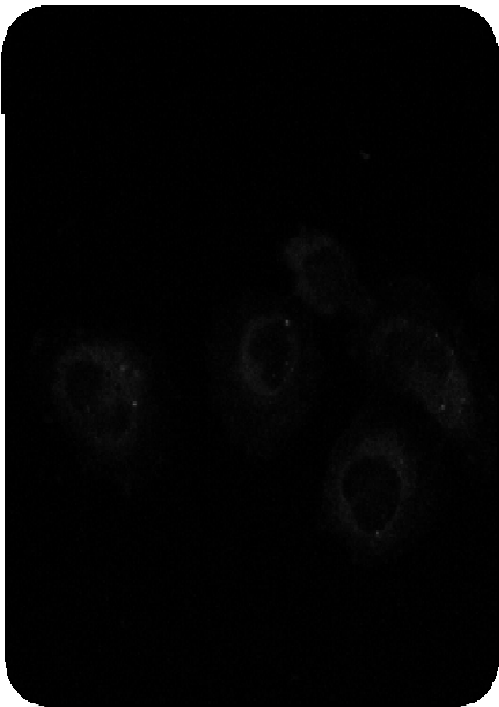
Polymeric Nanoparticles: synthesis and characterization



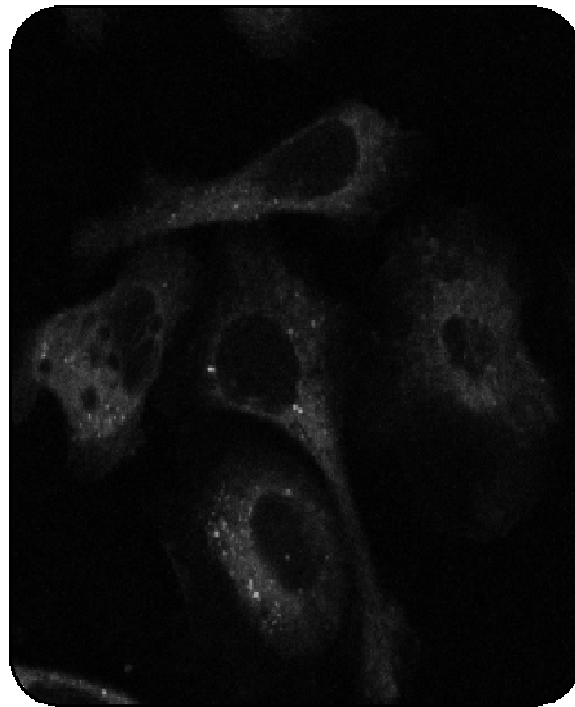
...our results

Nano-curcumin uptake *in vitro*

Free curcumin



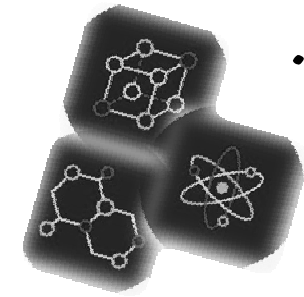
Nano-curcumin



Caco-2 Cells treated with nano-curcumin showed an increase in fluorescence (green) and, thus cellular uptake, when compared with cells that were treated with non-encapsulated curcumin (free curcumin).

Fluorescence was detected under a fluorescence microscope with a GFP filter due to curcumin's auto-fluorescent property. All representative images had similar numbers of cells.

Polymeric Nanoparticles: synthesis and characterization



...our results

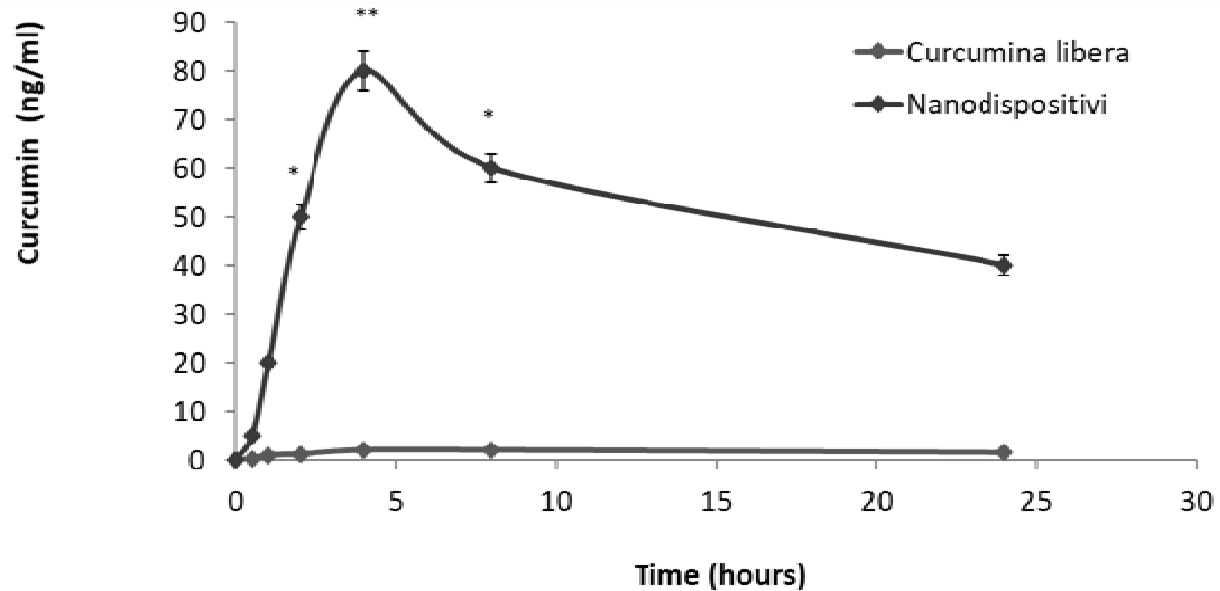
Protocol:

- Single oral dose administered;
- M/F healthy volunteers, aged between 18 and 55 years, BMI between 18.5 and 29.9 Kg/m²;

Sample collection:

- time points of 0 (pre-dose)
 - 1 hour
 - 2 hours
 - 4 hours
 - 8 hours
 - 24 hours
- post-oral dose administration

Pharmacokinetic assay



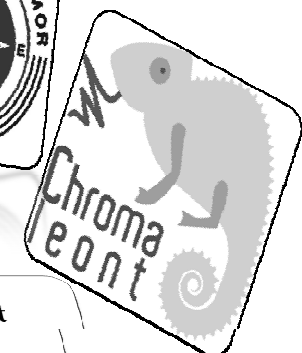
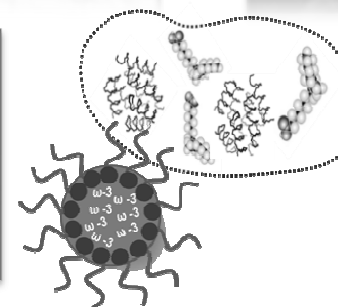
Compared with free drug, the plasma levels of curcumin were remarkable higher (~20-fold) after administration of nano-curcumin than free curcumin from 1 to 24 time points. The difference was most evident at time points 4 and 8 ($p < 0,05$). The results demonstrate that nano-curcumin were able to improve bioavailability of poorly water soluble drugs.

Nanotechnology-based delivery approach



Avantech
Tools for the future

Nanocarrier identification to improve the solubility and bioavailability of curcumin and other bioactive molecules (*i.e. marine bioactive compounds*)



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• Damor,
Pharmaceutical
s Napoli

• Avantech Group
s.r.l. Angri
(SA)

• Chromaleont
s.r.l.. Food
Analytical
Methods.
Messina

European Research & Innovation Project,
EC, 2015
MISE_Horizon 2016



2 projects

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The team of Neurologists, cooks & alchemists

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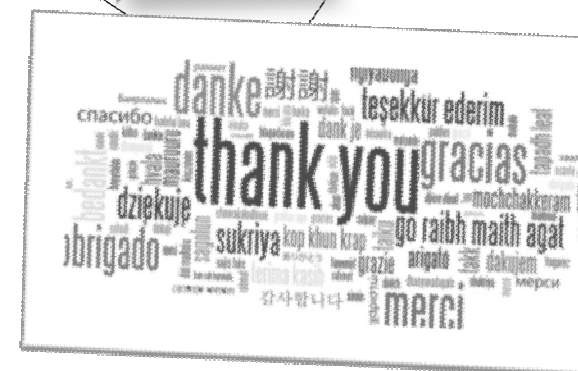


National Research
Council of Italy

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