Nutraceuticals and Functional Foods to achieve a Functional Diet.

An overview on Nutrheff (*Nutraceutical Health Enhancing Functional Foods*), the CNR network on nutraceutical and functional food research.

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CNR is the greatest public research organization of Italy. It was founded in 1923.

CNR is composed by 7 Departments, 102 Institutes, Researchers: > 4,000

The average (per year) budget: € 900 million
About 40% from external funds (contracts with private entities)

Departments

Earth system science and environmental technologies
Biology, agriculture and food sciences
Chemical sciences and materials technology
Physical sciences and technologies of matter
Biomedical sciences
Engineering, ICT and technologies for energy and transportation
Social sciences and humanities, cultural heritage
- Collect and connect the know-how in basic sciences and applied research
- Enhance coordination of specialized individual expertises
- Sustain the industrial production and promote commercial opportunities

**Functional Foods**
Probiotics and functionalised foods
20 groups

**Nutraceuticals**
Characterization of bioactive molecules
29 groups

**Biological Validation**
In vitro, in vivo, in silico models
33 groups

**Dissemination and Technology Transfer**
Communicating new knowledge
8 groups

**Quality and Safety**
Innovative methods for monitoring; consumer science
26 groups

**The Network**
Department of Biology, agriculture and food sciences
Factors affecting the development of the world market

- Growth of health care costs: interest in preventive healthcare and increase of self-medication;
- Interest for functional food designed for personalized nutrition
- Functional attribute to foods as a marketing strategy: increase in research and technological needs of food industry;
- Scientific demonstration to meet claim regulation.
#1  **Nutraceuticals in foods** – identification and investigation on complex matrices/bioaccessibility/bioavailability

#2  Scientific evidences on the **relationships between a food and well-being/reduction of disease**

#3  **Quality and safety** of components and functional foods

#4  **Interplay** between bioactive **components** and gut **microbiota**

#5  **Technological solutions** for **functionalized foods** with high level of consumer satisfactions
Can the bioactive compounds from complex food matrix really contribute to achieve a functional diet?

Actions of polyphenols in *in vitro* and in animal studies

**Body weight**
- Energy expenditure
- Lipogenesis
- Fat mass

**Fat metabolism**
- HDL
- VLDL

**Glucose Metabolism**
- Digestion and absorption
- Insulin secretion
- Insulin sensitivity

**Inflammation**
- IL-5, TNF-a
- Endothelial
- NO Platelets activation

**Blood pressure**

**Oxidative stress**

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Polyphenols from artichoke heads (Cynara cardunculus (L.) subsp. scolymus Hayek): in vitro bio-accessibility, intestinal uptake and bioavailability

Isabella D’Antuono, Antonella Garbetta, Vito Linsalata, Fiorenza Minervini and Angela Cardinali*

**(Poly) phenol from Food Matrix**

High relative **bioaccessibility** since the 50-70% of their initial content can reach the intestinal epithelia

Digestive release in GI tract

**Chlorogenic acid**

3,5-O-dicaffeoylquinic acid

1,5-O-dicaffeoylquinic acid

Apigenin 7-Glucoside

Uptake by Caco-2

Very low **bioavailability** (0.1%) as predicted by intestinal absorption (according to the poor uptake of dietary polyphenols)

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EFFECT OF PROCESSES ON THE BIOAVAILABILITY OF SELECTED NUTRIENTS/BIOMOLECULES

Complete meal of food models

Multicatheterized minipigs

Tomato - lycopene from tomato purée or its metabolites were not detected in plasma

Design and development of REAListic food Models with well characterized micro- and macro-structure and composition

Didier Remond@clermont.inra.fr
A randomised, two-way cross-over study

10 healthy adults consumed either a test meal:

- **19-mg (all-E)-LYC** from tomato paste
- same meal plus 500-mg **calcium carbonate** as a supplement.

**RESULTS**

LYC bioavailability was diminished by **83%** following the addition of Ca in the test meal

Reduced bioavailability could be related to **the electrical charge of LYC micelles in presence of Ca.**
POLYPHENOL-RICH DIETS

*Dietary intervention to achieve the target “functional diet”*

Randomized controlled study involving 86 overweight/obese individuals with metabolic alterations consuming diets naturally rich in polyphenols (2.5 g/die – from green tea, onions, rocket etc.; 8 wks)

**Reduction of** postprandial triglycerides rich lipoprotein levels (independent cardiovascular disease risk factor) (Annuzzi G et al, Am J Clin Nutr., 2014)

**Reduction** of postprandial blood glucose and increasing early insulin secretion (Bozzetto et al., Diabetologia, 58, 2015).

Through their effects on postprandial lipemia and oxidative stress, *polyphenol-rich* foods may favorably affect cardiovascular disease risk.

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Clementine and mandarin juices have the potential for drug interactions by:

- modulating several drug transporters and drug metabolizing enzymes

Evidence from *in vitro* and *in vivo* studies has indicated that the constituents of herbal preparation, even food, interact with various *drug metabolic enzymes (CYP450)* extensively.

A number of dietary components are known to inhibit the CYP3A4 system.
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La Marca et al. Food Chemical Toxicology 2012
A number of dietary components are known to inhibit the CYP3A4 system. Evidence from in vitro and in vivo studies has indicated that the constituents of herbal preparation, even food, interact with various drug metabolic enzymes (CYP450) extensively.

On the basis of their concentration ITCs:

- can have a protective effect by activation of regulated genes activating detoxifying enzymes
- have the potential to inhibit, at least in rat liver, the CYP3A2 catalysis leading to a possible toxic effect.

La Marca et al. Food Chemical Toxicology 2012
The interaction between microbiota and food bioactive compounds is a reciprocal correspondence.

Knowledge of the **interactions between bioactive** food compounds and **specific intestinal microorganisms** could contribute to a better understanding of both positive and negative **interactions in vivo**.
Gut Microbiota and Polyphenols: A Strict Connection Enhancing Human Health

Filomena Nazzaro¹, Florinda Fratiampi², Antonio d’Acicrane¹, and Raffaele Coppola²,²

¹ Institute of Food Systems, CNR-ISMN, Via Roma, 04, 55100, Livorno, Italy
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Figure 20.1 Metabolism and catabolism of polyphenols during and after digestion.
Fungal Populations of the Human GI Tract

Fungal component of the human gut microbiota has been neglected for long time.

Recently, the combination of metagenomics and fungal cultivation allowed an in-depth understanding of the fungal intestinal community structure associated to the healthy status.

*No information* are available on a possible reciprocal correspondence nutraceuticals/mycobiota.
Molecular mechanisms of cell stress response in yeast *Saccharomyces cerevisiae*, with a particular focus on the role of mitochondria in the integration of environmental clues and intracellular signaling in the regulation of cell death, survival and ageing.

The challenge is to identify key mechanisms/cell components involved in:

- biological activity of natural and synthetic compounds to design new drugs and/or nutraceuticals
- fungal-microbe interactions in microbiota
- fungal community response to micro-environment changes
Gluten detoxification by enzyme treatment of wheat flour
Gliadin cross-linking (transamidation)

The enzyme reaction

Microbial transglutaminase

LQLQPFPQPQLPY
+ lysine alkyl ester

The functional food

control

transamidated

>70,000 ppm

5.8 ppm

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A Randomized, Controlled Clinical Study demonstrated that reintroduction of Gluten Following Flour Transamidation is possible in Adult Celiac Patients

Fig: Histological appearance of intestinal mucosa from a CD subject at baseline (a) and following a 90-day (K-CH3)-transamidated gluten challenge
NON CONVENTIONAL RTE PROBIOTIC FOODS FOR GUT MICROBIOTA MANIPULATION

CONVENTIONAL FOODS

- table olives, artichokes, cabbage, fish fillets

FUNCTIONAL FOODS

- Biotechnology
- high organoleptic quality

*Lactobacillus paracasei* LMG P-22043

CNR-ISP A

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NON CONVENTIONAL RTE PROBIOTIC FOODS FOR GUT MICROBIOTA MANIPULATION

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Lactobacillus paracasei LMG P-22043

A portion of artichokes or table olives or cabbage or fish fillet can carry more than 1 BILLION LIVE AND ACTIVE LACTOBACILLUS PARACASEI LMG-P22043 amount comparable or greater than those of milk-based products

Vegetable and fish matrix support:

- Long lasting strain survival
- Gut colonization
- Improvement of functional constipation

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Randomised clinical trial: efficacy of *Lactobacillus paracasei*-enriched artichokes in the treatment of patients with functional constipation – a double-blind, controlled, crossover study

G. Riezzo*, A. Orlando†, B. D’Attoma†, V. Guerra†, F. Valerio†, P. Lavermicocca†, S. De Candia† & F. Russo†,†

The sample size calculation:

80% power at a two-sided significance level of 5%.

19 pzs were required to reveal a treatment preference of 80% for probiotic-enriched artichokes respect to 20%.

Clinical trial NCT01212146
A diet with probiotic enriched-artichokes:

- Allows strain colonization of the human gut
- Improves microbiological intestinal parameters
  - improving LAB number and diversity
  - lowering potential harmful bacteria
  - modulation of faecal enzymes
  - modulation of SCFA production
- Reduces GI-Symptom Rating scores (Rome Criteria III):
  - feeling of incomplete evacuation
  - decreased passage of stools
  - abdominal distension
- Improves stool consistency

Clinical trial NCT01212146
The growth of the functional foods sector can provide significant benefits to human health and offers opportunities for the agri-food industry.

Considering that the high costs of development, the uncertainty of the investment return and the complexity of claims and regulatory items are obstacles for FF innovation, research efforts should:

- Apply rigorous scientific approach producing highly significant demonstrations of efficacy (based on nutrigenomic and nutrigenetic evidences)
- Reinforce the dialogue between regulatory authorities, researchers, nutritionists and scientists in industry
- Include FF and nutraceuticals in new dietetic guidelines for better nutrition and personalized nutrition
- Improve communication of health benefits for a consumer understanding of the claim itself.

Expertises and facilities of CNR NUTRHEFF are available for building cooperative actions to improve the current knowledge and support the agri-food sector for development of Functional foods.
A practical guide for cancer patients and family members during chemo-therapies

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03.30-05.00 p.m.
NUTRHEFF-CNR (NUTRACEUTICAL HEALTH ENANCING FUNCTIONAL FOOD)

12.00-12.45 a.m.
ORAL COMMUNICATIONS
Nutrheff - CNR hot topics: food bioactive compounds and health
Thank you for your attention

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FUNCTIONAL FOODS