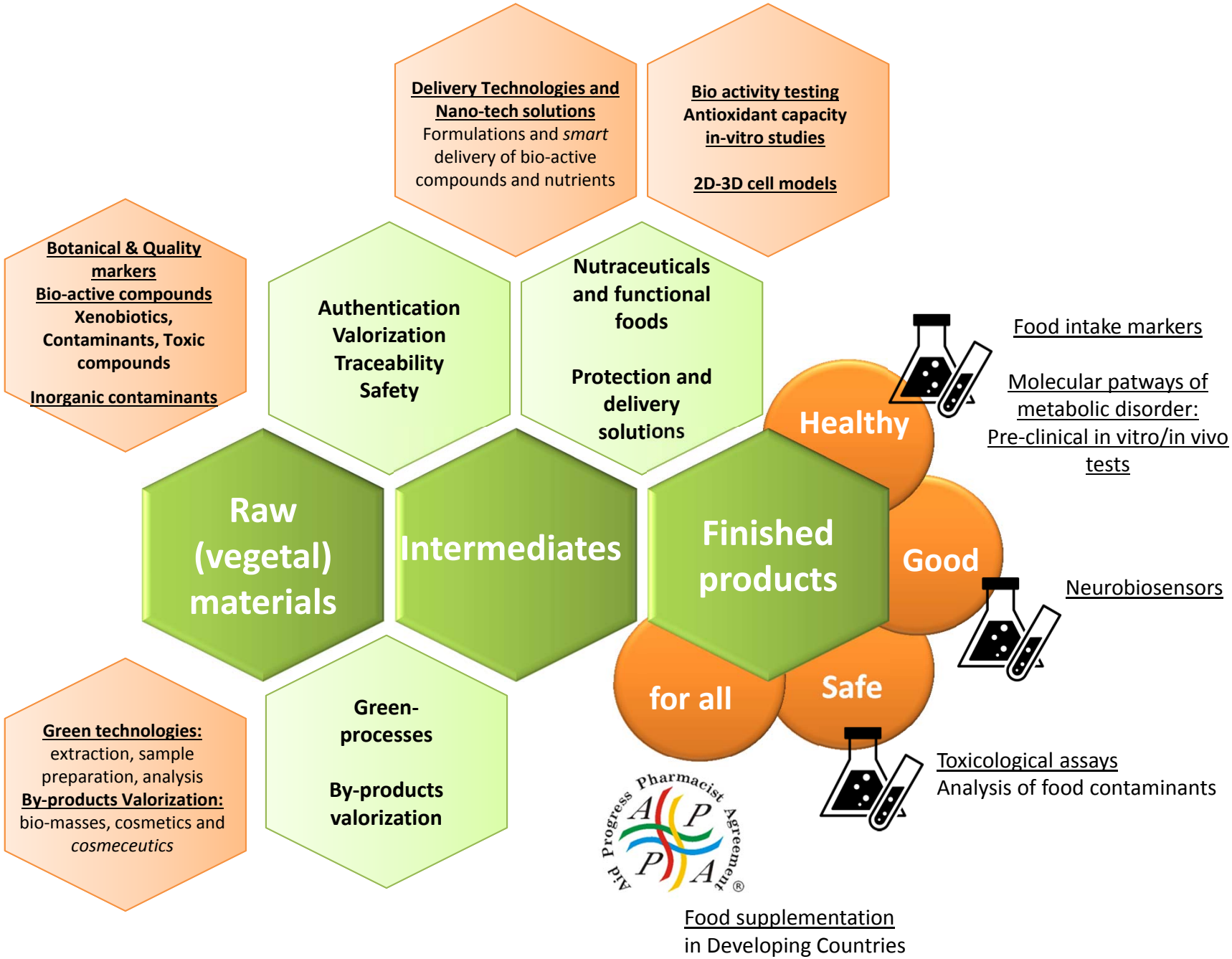
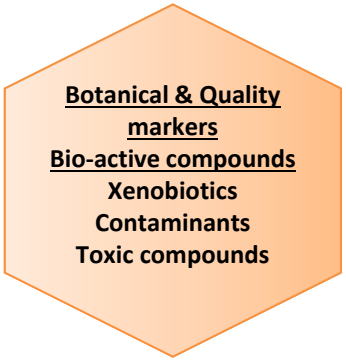
Ali(medica)menta® is a interdisciplinary research platform (network) within the Department of Drug Science and Technology at the University of Turin aimed to synergically combine different disciplines and expertise around healthy food topics, mainly vegetal products and their quality and safety.

The platform offers expertise and facilities to study the different aspects along the food transformation chain by focusing on bio-active components (nutrients, secondary metabolites, nutraceuticals and sensory active compounds).

In particular, the research activities deal with the most recent innovation and technological achievements in the extraction/preparation of vegetal raw materials, removal of undesirable components, valorization and modification of food composition and development of novel products.

Consistent with the expanded role for Pharmacists in Public Health, special attention is paid to the correlation between Food and Health helping to promote healthy diets and lifestyles.


Delivery Technologies and Nano-tech solutions
Formulations and *smart* delivery of bio-active compounds and nutrients
Bio activity testing
Antioxidant capacity
in-vitro studies
2D-3D cell models
Botanical & Quality markers
Bio-active compounds
Xenobiotics, Contaminants, Toxic compounds
Inorganic contaminants
Authentication
Valorization
Traceability
Safety
Nutraceuticals and functional foods
Protection and delivery solutions
Raw (vegetal) materials
Intermediates
Finished products
Healthy
Good
for all
Safe
Food intake markers
Molecular patways of metabolic disorder:
Pre-clinical in vitro/in vivo tests
Neurobiosensors
Toxicological assays
Analysis of food contaminants
Green technologies:
extraction, sample preparation, analysis
By-products Valorization:
bio-masses, cosmetics and *cosmeceutics*
Green-processes
By-products valorization
Aid Progress Pharmacist Agreement
Food supplementation
in Developing Countries



Ensuring a "food global quality" from raw materials to end products

The final research objective is to ensure a "food global quality" from raw materials to end products, including: botanical and geographical fingerprint, nutritional profile, sensory quality, presence of bioactive compounds and safety aspects (residues and contaminants, adulterations, toxic compounds). The research group competences deal with: development and validation of innovative, reliable and automated analytical methods to define the food sample fingerprint as a chemical tool for integrity assessment.

Facilities, technologies: Analytical approaches for known markers and untargeted fingerprinting methods based on multidimensional and hyphenated analytical platforms (GC-MS/FPD, Fast-ES-GC-MS and GCxGC-MS/FID, LC-UV/DAD and LC-MS/MS) coupled with miniaturized, eco-friendly sample preparation techniques. Chemometrics and data mining tools complete team's skills.

Principal Investigator: Prof. Rubiolo Patrizia

<u>Green technologies:</u>
extraction, sample preparation, analysis
<u>By-products Valorization</u>:
bio-masses, cosmetics and *cosmeceutics*

Green extraction and biomass valorization toward value-added food ingredients

Following the biorefinery concept agro-food industry is searching innovative technologies for green extraction and to recover from bio-waste useful ingredients. This requires the development of enabling technologies for process intensification to make the process economically profitable. Bio-waste is generally a negative-cost feedstock for the potential production of high value-added products and bioenergy. Some example of our goal are the full valorization of biomass in the production of tomatoes sauce, fruit juices and chocolate. This investigation is already active in partnership with big industrial partners.

Facilities, technologies: A list of enabling technologies and processes with Lab and pilot scale reactors for green extraction by means of high-intensity ultrasound, hydrodynamic cavitation, microwaves, ball mills. This is supported by a full analytical support (GC-MS, GC-Head Space, LC-UV/DAD/ELS, LC-MS, NMR etc.).

Principal Investigator: Dr. Arianna Binello, Dr. Luisa Boffa, Prof. Giancarlo Cravotto

Delivery Technologies and Nano-tech solutions
Formulations and *smart* delivery of bio-active compounds and nutrients

Nutritional and health technology and nanotechnology

Our aim is to encapsulate in suitable delivery systems microelements, nutrients and food actives, with stability, solubility and/or uptake problems. Moreover, these systems can be used also for taste masking purposes. The encapsulation offers several advantages: protects from chemical or biological degradation during processing, storage and utilization, targets the release to the desired site of action (i.e. employing gastroresistant polymers to reach the colon), modulates taste, flavor, texture (i.e. obtain foods with limited salt/sugar/fat).

The mainly delivery systems studied are micellar solutions, micro/nanoemulsions, self-emulsifying drug delivery systems, liposomes, nanoparticles, nanodispersions, cyclodextrin complexes and derivatives.
Different analytical technique are available to evaluate the influence of each carrier on the stability and efficiency of the included molecules: the physico-chemical stability can be monitored in several conditions of temperature, pH, UV-Vis irradiation meanwhile release and activity of guest compounds can be tested through different *in vitro* studies.

Facilities, technologies: HPLC systems integrated with UV-Vis, fluorescence, evaporative light scattering and diode array detectors; Multi Flow FFF analyzer; High-pressure homogenizer; Optical microscope, Freeze dryer; Thermal analyser (DSC); Particle size and Zeta potential instrument (DLS); Rheometer

Principal Investigator: Prof. Roberta Cavalli

Biocompatible lipid nanosuspensions can be effectively used to increase the intestinal uptake, by using the intestinal lymphatic uptake strategies: this is much more important when normal intestinal uptake is compromised, like in elder people, or in people suffering from different intestinal uptake diseases.

In this context, biocompatible solid lipid nanoparticles (SLN) can be a suitable alternative: the so called fatty acid coacervation technique, developed by Dr. Luigi Battaglia and co-workers, has the advantage, over conventional SLN preparation methods, to avoid toxic solvents, as well as to operate at mild temperatures. This is useful for food industry, in particular for those microelements that suffer from thermal instability.

Principal Investigator: Dr. Luigi Battaglia

Bio activity testing
Antioxidant capacity
in-vitro studies

Antioxidant activity of food compounds

In vitro biological screening

Biological screening of nutraceutical candidates can be performed by:

1) full characterization, through in vitro biological and pharmacological assays of either synthetic derivatives or natural extracts from vegetal sources. (ORAC and TEAC assays, DPPH reactivity, inhibition of lipid peroxidation or dienes conjugate formation, measurements of phenols, tannins and carotenoids).

2) evaluation of the effects of dietary supplements ingestion on oxidative stress biomarkers in biological fluids (urinary 15-F2t-isoprostanes, serum oxLDL, serum glutathione indexes, plasmatic TBARS and FRAP).

Facilities, technologies: Perkin Elmer multimode plate reader able to read spectrophotometric, fluorescent or luminescent assays, Ultracentrifuge

Principal Investigator: Prof. Clara Cena

Bio activity testing
Antioxidant capacity
2D-3D cell models

Effect on hypoxic stress in cell culture

Our aim is to evaluate the antioxidant activity of new compounds, mainly from vegetable extracts, in in vitro two- and three-dimensional (2D and 3D) cell culture models. Our approach is based first on the evaluation of the cell viability to determine the cytotoxic effect of the vegetable extracts (IC50). A hypoxic stress will be induced to test the antioxidant activity of the vegetable extracts by evaluating the free radical species production with a flow cytometer analysis. The radical species production will be evaluated with the vegetable extract added either before or during the hypoxic stress. Molecular mechanisms, induced or inhibited by the antioxidant effect of the vegetable extracts, will be investigated by gene expression analysis in our suspension/monolayer (2D) or multicellular spheroids (3D) cell cultures.

Principal Investigator: Prof. Valentina Carabelli, Dr. Roberto Canaparo

Food intake markers (Foodomics, Sensomics and Metabolomics)

The research team works within the “food-omics” domain (Foodomics, Sensomics and Metabolomics) by developing profiling and fingerprinting methodologies for chemical characterization of complex food samples including: primary and secondary metabolites, fermentation products and technological markers, sensory active compounds and biologically active compounds (nutrients and non-nutrients). The study of food intake markers in biological fluids (urine, plasma and tissues) after dietary intervention studies are part of an active collaboration with pharmacologist, pathologist and nutritionists within UniTO.

Facilities, technologies: Advanced separation platforms (mono and multidimensional gas chromatography and liquid chromatography); hyphenated techniques including MS and MS/MS, olfactometry, element specific detectors (SSD) and other GC detectors (FID), integrated/automated and solvent-free sample preparation. Data interpretation includes the development of advanced algorithms for profiling and fingerprinting aided by chemometrics.

Principal Investigator: Prof. Chiara Emilia Irma Cordero

Molecular patways of metabolic disorder: Pre-clinical in vitro/in vivo tests
Impact of food components on non-communicable diseases

Development of pre-clinical in vitro and in vivo models of non-communicable diseases, mainly diet-induced metabolic disorders, for the evaluation of the effects of chronic exposure to food components. Validation of new markers for a better timely diagnosis and constant monitoring of non-communicable diseases. Activation and/or modulation of selective receptors and molecular pathways involved in the pathogenesis of non-communicable diseases are evaluated in cell lines (in vitro experiments) or tissues and organs (in vivo experiments) in the presence or absence of chronic exposure to selected food components. Data on biofluids of patients are collected and compared to pre-clinical results.

Facilities, technologies: A recently renovated animal house, lab equipment for cell cultures, molecular, biochemical and histological analysis, including Western blot analysis, rt-PCR, immunohistochemistry, enzymatic assays, cell proliferation assays, inverted, confocal microscopes connected to digital camera with computerized microimaging analysis system.

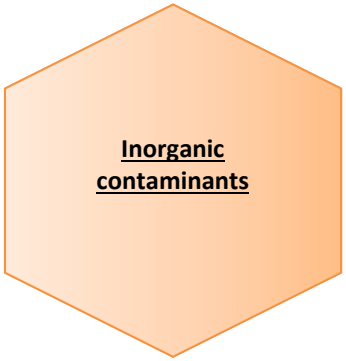
Principal Investigator: Prof. Massimo Collino, Dr. Simonetta Oliaro Bosso

<u>Neuro-biosensors</u> for detecting active odorant and taste molecules on microelectrode arrays (MEAs)

There is great interest in the identification of odorant molecules to be associated with eatable products to improve food quality, attractiveness and consumption. To test on a large scale the response of odorant receptors (ORs) to a variety of molecules we plan to develop an artificial bio-sensing system (bio-electronic nose) based on cultured neurons on which ORs and cAMP-activated channels are transfected. The tight coupling of ORs and cAMP-activated channels is expected to cause resting depolarization of living neurons and subsequent spontaneous firing in response to an odorant molecule. Recording of action potential firings on transfected neurons dispersed on a recording MEA system should thus give direct information of the OR response to distinct odorants. The development of this novel "bio-electronic nose" should allow large-scale screening of odorant molecules to be associated with food products.

Facilities, technologies: 64 Microelectrode Array (MEA) system equipped with stereomicroscope, temperature control and Neuroexplorer software for action potential bursts analysis. Fully equipped tissue culture service for preparing and maintaining long-term clonal and primary cell cultures.

Principal Investigator: Prof. Emilio Carbone, Dr. Andrea Marcantoni



<u>Toxicological assays</u>: analysis of diagnostic inorganic elements even at trace and ultra-trace levels as food contaminants

The concentration and the distribution of inorganics (nutrients, metals, rare earths, isotopic ratios) in vegetal foods depends on a number of variables, such as climate, soil characteristics, transportation, storage, transformation and it can be used for geographical assessment. For these reason, we will quantify the presence of diagnostic inorganic elements even at trace and ultra-trace levels. A complete inorganic profile will be obtained for geographical origin authentication, to study essential nutrients distribution through the entire product life and to detect possible contaminations both in raw materials and finished products.
We could characterize i) the total content of metals, rare earths and other inorganic components; ii) the agricultural lands from a phisical (pH, humidity, grain size distribution) and chemical point of view. We could control the level of possible inorganic contaminants present in soils, waters and particulate matter that can contribute to the quality of the vegetables.

Facilities, technologies: High Resolution Inductively Coupled Plasma Mass Spectrometer (HR-ICP-MS); Inductively Coupled Plasma Optical Emission Spectrometer (ICP-OES); Atomic Absorption Spectrometer with Graphite Furnace (AAS-GF); voltammetric analysers with hanging mercury drop electrodes and/or solid/micro/nanostructured electrodes; microwave digestion systems

Principal Investigator: Dr. Agnese Giacomino

Support to effective and functional galenic lab in hospitals located in Developing Countries, including food supplementation against the malnutrition

The A.P.P.A.® Project is structured in six phases, through which it is possible to obtain an effective and functional galenic lab in hospitals located in DCs. Several Projects are working on: two in Cameroun, Madagascar and Angola; one in Chad, Haiti and Zimbabwe. A.P.P.A.® labs production concerned mainly medicinal products but often we received many requests to set up preparations suitable for food supplementation against the malnutrition.

Methodological approach: In agreement whit local medical doctors the active molecules are chosen and then the preparations are formulated: liquid oral formulations are preferred for infants and children. Moreover, appropriate excipients must be selected for pregnant women, infants and children. Each preparation have been tested to check its quality and its stability.

Facilities, technologies: Lab equipment for preparation of sterile and non-sterile galenic medicinal products; equipment required by the European Pharmacopoeia for quality control tests (disintegration, dissolution, uniformity of mass, uniformity of content, friability, resistance to crushing, dissolution), UV-Vis spectrophotometer, HPLC.

Principal Investigator: Prof. Paola Brusa