

**ABSTRACTS** 

We are honored to present you to the workshop proceeding of "Nutraceuticals and functional foods, Scienze & Industry" which was organized on February 3, 2023 in Palermo

# **PROGRAM**

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9:00 - 9:45 Registrazione dei partecipanti

9:45 Apertura dei lavori Domenico Nuzzo, Antonella Amato, Manfredi Rizzo

Saluti Istituzionali



Chairman, Antonella Amato e Manfredi Rizzo

10.00 Mario Allegra — Analisi biochimiche come strumenti per la valutazione dell'impatto dei fitocomposti sulla salute umana

10.20 Antonella Amato - Fitocomposti e cibi funzionali: effetti anti-obesità in un modello animale e presentazione del

Corso di Perfezionamento

10.40 Maria Grazia Zizzo - Molecole bioattive delle alghe contro le IBD

11.00 Coffee Break

11.30 Manfredi Rizzo - Gli studi traslazionali: applicabilità terapeutica degli integratori contro le patologie non trasmissibili

11.50 Fabio Caradonna — La ricerca sperimentale come mezzo per l'innovazione di prodotti già esistenti: testimonianza sul campo

12.10 Domenico Nuzzo — Strategie e valorizzazione degli esuberi della filiera agroalimentare ai fini salutistici e presentazione tavolo strategico

12:30 Francesco Cappitelli (online) - Strategie formulative per un integratore efficace e di successo

12.50 Light Lunch



Chairman, Domenico Nuzzo e Paolo Colombo

14.00 Barbara Angelini (online) - Strumenti di Trasferimento Tecnologico del CNR

14.20 Alberto Firenze - Strategie e progettualità per la valorizzazione della dieta mediterranea

14:40 Enrico Camilleri - M&D, Il finaziamento dei progetti di ricerca, sviluppo e innovazione: esperienze ed opportunità

15.00 Fabio D'Elia (online) - Food Hub, Facilitare l'innovazione nell'agroalimentare come mezzo per promuovere il progresso

15:20 Federico Casotto (online) - Design Group Italia, La fabbrica del cibo, progettare green food

15.40 Stefania Raimondo - Navhetec, Nanosoluzioni in nutraceutica: Navhetec, dal laborarorio all'impresa

16.00 Riccardo Bottiroli (online) - Developeat , Cibo del futuro e nuove frontiere del Food Tech



Chairman, Alberto Firenze

16.20 Momento di confronto tra CNR-Università ed Aziende. Prendono parola alcune aziende

Chiusura Lavori

17.00 Light Coffee Break di saluto

# Nutraceuticals: a source of benefit for cardiovascular risk

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#### Abstract

The term "nutraceutical" comes from the union of the words "nutrient" and "pharmaceutical" and indicates substances of natural extraction (mostly vegetable) with pharmacological actions demonstrated in modulating specific functions of the organism in a physiological/healthy sense. These could be used as supplements in the daily diet due to their easy availability and their beneficial properties, such as polyphenols, omega-3 fatty acids, macroelements, vitamins, red yeast rice, bergamot, berberine, artichoke, soluble fiber, plant sterols and stanols alone or in combination with each other. The main nutraceutical supplements perform fundamental functions for the body and are used to: 1) Strengthen the immune system, 2) Regularize the gastro-intestinal functions, 3) Support the body during physical activity, 4) Help improve certain bodily functions, 5) Delay the aging process, 6) Prevent chronic diseases, and 7) Significantly reduce the risk of developing degenerative or cardiovascular diseases.

Recent clinical trials have shown that some nutraceuticals can be active on modifiable cardiovascular risk factors (obesity, hypertension, hyperlipidemia, diabetes mellitus, metabolic syndrome) with different types of mechanisms.

These nutraceuticals could exert significant lipid-lowering activity including improvement of endothelial dysfunction and arterial stiffness, as well as anti-inflammatory, antithrombotic, antioxidant or antiapoptotic properties.

The study of the beneficial effects of nutraceuticals in patients, including product standardization, duration of supplementation and definition of optimal dosing, could help better define appropriate treatment. It is expected that ongoing and future studies will confirm the benefit on reduced overall CV risk and long-term safety and effectiveness against clinical outcomes.

#### Keywords

Cardiovascular risk, Metabolic Syndrome, Nutraceuticals.

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# Green extraction from carrot and pumpkin for food and dietary supplement

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#### Abstract

Supercritical CO2 (SFE) extraction technology is an excellent alternative to conventional solvent extraction (CSE). It represents an environmentally friendly, non-toxic technique for obtaining food-grade solvent-free extracts from plant materials (Durante et al. 2016). Carrot roots and pumpkin peponides are rich sources of -carotene, precursor of vitamin A, and other bioactive compounds suitable as high quality ingredients in the formulation of supplemented food and nutraceuticals (Durante et al. 2012; 2020). Here, the lipophilic phytocomplexes obtained by SFE and CSE from carrot and pumpkin matrices impregnated with organic hempseed or flaxseed oils as co-solvents were tested in vitro to explore the possible effects of 1) plant source, 2) co-solvent composition, and 3) extraction method on the ability to counteract inflammatory and oxidative processes associated with the onset of several pathologies. The extracts showed different quali-quantitative composition of bioactives, including tocochromanols and carotenoids, as well as healthy lipid indices. The anti-inflammatory activity of the extracts was analyzed by assessing their ability to modulate nitrite oxide production (NPlps) in lipopolysaccharide (LPS)-stimulated RAW 264.7 macrophages. A dose-dependent anti-inflammatory potential of carrot and pumpkin extracts (CPex) was observed, as well as their ability to decrease the expression levels of several pro-inflammatory cytokines. All extracts interfered with the pro-inflammatory effects of MDA-MB-231 breast cancer cell-conditioned media. Furthermore, CPex inhibited reactive oxygen species (ROS) accumulation in LPS-stimulated macrophages. The nuclear factor erythroid 2 related factor 2, a transcription factor, proved to be involved in the mechanisms underlying such effects; its activation by carrot extracts was corroborated by the increase in mRNA levels of several target genes, such as catalase and glutathione-peroxidase. Regardless of matrices, co-solvents and extraction method, -tocopherol, lutein, carotenes and total carotenoids negatively correlated with NPlps, and most carotenoids and their total negatively correlated with the intracellular ROS levels, while positive correlation was found between total tocopherols/total carotenoids ratio and NPIps and ROS production. These results suggest an idiosyncratic effect of the pool of bioactives in the CPex on inflammation-induced oxidative stress, emphasizing the importance of the interaction among plant extract constituents in antioxidant/anti-inflammatory cellular response and the importance of ingredient' choice (source and production technology) in food

#### Keywords

supplementation.

carotenoids; bioactive compounds, MDA-MB-231 cell-conditioned media, nitric oxide production, nuclear factor-erythroid-2-related factor 2, tocochromanols.

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# Experimental research as a means for the innovation of already existing products: reporting of a type-case

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#### Abstract

Innovation and the creation of new products in a company, or in a food industry, is an expensive process and requires profound transformations of the production processes. For this reason, the governance of some businesses often gives up on the idea of innovating, especially if some of their products, driving the market, can ensure short and medium-term earnings security.

It is also quite well known, however, that the long-term solidity of a company is ensured only by innovation: mediating between these two possibilities is very difficult but one sustainable possibility, today, may consist in functionalizing already existing food products, adding, in the industrial manufacturing process, bioactive and healthy substances in order to increase the nutritional value of the product, adding beneficial effects for human health and thus reducing the transformations of production processes to a minimum. Experimental research can make this idea feasible by refining concentrations of the bioactive molecule(s), physicochemical parameters and functionality analyses. Various examples can be reported of company-university collaborations aimed at this form of innovation. The one that involved my lab refers to a food product for children that has been functionalized with Bronte pistachio extract. In this specific case, our experimental research has demonstrated the maintenance of bioactive activities of the functional extract downstream of the food production process. Furthermore, in vitro studies, on cell models that simulated human intestinal tissue, demonstrated the beneficial capability of pistachio extract to modulate the cell DNA damage induced by mutagens and/or epimutagens, characteristics that we have also been found in other vegetables molecules with the same nutrigenomic effects (Volpes et al., 2023). In conclusion, we propose the functionalization of already existing foods as a sustainable form of innovation that with few modifications of manufacturing processes, can generate "new" food products with at least two advantages: nutritional and healthy.

#### Keywords

Nutrigenomics, Epigenetics, Functionalization, Nutrition, Innovation.

#### References

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## Neuroprotection by nature-inspired mitochondria-targeted phenolic derivatives

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#### Abstract

Neurological disorders (ND) are the leading cause of long-term disability and the second leading cause of death in the world. ND and related diseases have an impact on the sustainability of the national health and social system. The absence of resolutive therapies and in part to the poor efficacy of preventive measures represent the necessity to develop new therapies and interventions. Oxidative stress, together with aging and genetic factors, plays an important role in the occurrence of neurodegenerative diseases like Alzheimer's, Parkinson's and Huntington's diseases. Targeting drugs to subcellular compartments represents one of the modern trends in molecular pharmacology. Mitochondria are vital intracellular organelles and play a key role in energy production and regulation of cell-stress pathways. Unbalanced mitochondrial oxidative stress determine cell damage such as lipid peroxidation, protein oxidation, and DNA lesions. Mitochondria have some unique characteristics that can be used for targeting, but one of the limiting factors of antioxidant therapy in the treatment of mitochondrial diseases has been the inability to improve the levels of antioxidants in the mitochondria. In this context, a collection of mitochondria-targeted derivatives was designed and synthesized by covalently linking a lipophilic cation to some selected natural antioxidants (i.e., coumaric acid, sinapic acid, syringic acid, ferulic acid, gallic acid, caffeic acid and rosmarinic acid). The synthesis was optimized under flow conditions, using cyrene (i.e., dihydrolevoglucosenone) as the solvent. Cyrene is an eco-friendly bio-available solvent useful to replace dipolar aprotic solvents which are in the REACH restricted substances list. A two-step continuous flow protocol was developed, and the desired MITO-compounds were isolated in moderate to good yields. To evaluate the biological activity, the natural and MITO- derivatives were tested on in vitro neuronal SH-SY5Y cells. The spectroscopic characteristics of these compounds were analyzed and by MTS assay the IC50 was calculated. The neuroprotection activity was evaluated and, in order to investigate the effect on the mitochondrion, the JC-1 assay was performed under the neurodegenerative stimulus. The data obtained show that the MITO-derived compounds are more efficient to protect mitochondrion from oxidative stress.

#### Keywords

Mitochondria protection, neurodegeneration, MITO-derived compounds

#### References

Pecora, D.; Annunziata, F.; Pegurri, S.; Picone, P.; Pinto, A.; Nuzzo, D.; Tamborini, L. Flow Synthesis of Nature-Inspired Mitochondria-Targeted Phenolic Derivatives as Potential Neuroprotective Agents. Antioxidants 2022, 11, 2160.

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## Phytochemicals and functional foods: anti-obesity effects in an animal model

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#### Abstract

Obesity is the most prevalent worldwide disorder and it is strongly linked to the metabolic syndrome (MetS), a cluster of disease risk factors including hypertension, dyslipidemia, fasting hyperglycemia or diabetes mellitus type 2 and brain impairments. Inflammation of adipose tissue in obese subjects plays a critical role in the pathogenesis of obesity-related complications. In fact, in obesity, the excessive adipose tissue becomes source of pro-inflammatory cytokines (tumor necrosis factor-alpha (TNF- ), interleukin (IL)-1, and IL-6), which in turn promote increased generation of Reactive Oxygen Species. Therefore, obesity is characterized by oxidative stress and pro-inflammatory processes.

Currently, there is no effective preventive or curative approach for metabolic syndrome. Weight loss (through an equilibrate diet) and increased energy expenditure (through physical activity) contribute to the prevention and treatment of MetS. Recent evidence suggests that some nutrients, foods, and dietary patterns have beneficial effects on MetS and improve metabolic profiles even in the absence of weight loss.

Consequently, the analysis of the potential beneficial effects of phytochemical or functional foods on obesity-related metabolic dysfunctions is emerging as a captivating aspect of the current research which captures the attention of the nutraceutical market. In this view, our research group using mice with diet-induced obesity explore the impact of natural compounds intake on different aspects of metabolic syndrome, such as glucose and lipid homeostasis, hepatic steatosis, adiposity, tissue, and systemic inflammation and oxidative stress, dysbiosis, and neurodegeneration. This animal represents a good model to analyse the potential beneficial effects of various treatments on obesity-related disorders, because when fed with a high-fat diet develops obesity and a progressive deterioration of metabolic control, characterized by hyperglycemia, insulin resistance, dyslipidemia, hepatic steatosis, systemic inflammation, neuroinflammation, and neurodegeneration. This presentation will summarize the results of the studies aimed at investigating the beneficial effects obtained by the consumption of pistachio, honey, and an extract of the alga Klamath on obesity metabolic disorders.

#### Keywords

obesity, dyslipidemia, diabetes, natural compounds

#### References

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# Antioxidant and anti-inflammatory role of grapefruit Integropectin

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#### Abstract

Rich in Citrus flavonoids and terpenes and retaining the highly bioactive rhamnogalacturonan RG-I region, IntegroPectin is a new family of pectins extracted from citrus processing waste via hydrodynamic cavitation in water only. Tested on microglia HMC3 cell line, grapefruit IntegroPectin was effective in protecting cells from death after exposure to oxidizing agents, reducing the amount of intracellular reactive oxygen species (ROS). Investigations on the mechanisms involved in grapefruit Integropectin-mediated protection unveiled the modulation of the apoptotic cascade and the downregulation of Caspase 3 activation. The analysis of the intracellular pathways activated by Integropectin indicated the specific involvement of PI3K/Akt pathway, a key regulator of survival during cellular stress. Moreover, the downregulation of inducible nitric oxide synthase expression also suggested that IntegroPectin may modulate inflammatory phenomena. These data, alongside preliminary results concerning the absence of toxicity of this new pectic biomolecule in peripheral blood mononuclear cells, suggest a potential therapeutic role of grapefruit IntegroPectin. Though preliminary, these results support experimentation on preclinical models of complex pathologies marked by extensive phenomena of oxidative stress and inflammation such as neurodegenerative diseases.

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# The impact of the Mediterranean Diet with high-polyphenol content extra-virgin olive oil intake on metabolic syndrome: preliminary results from a double-blind clinical trial

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#### Abstract

The Mediterranean Diet (MD) has protective effects against mortality and for cardiovascular event-free survival1. One of the added values of the MD is extra-virgin olive oil (EVOO), a food with monounsaturated fatty acids and high polyphenol content2,3. We evaluated the efficacy of the intake of high-polyphenol content EVOO (high polyphenols EVOO, HPPE) on clinical and laboratory parameters related to cardiovascular risk, metabolism, and liver function in two groups of metabolic syndrome (MS)/metabolic-associated fatty liver disease (MAFLD) patients. Here, we present the preliminary results of the 1st-year of a 3-year study co-financed by the European Union - PON Research and Innovation 2014-2020 - DM1062/2021. Thirty consecutive MS/MAFLD patients were enrolled at University Hospital of Palermo and randomized, in a single-center double-blind prospective study, to add HPPE or standard EVOO (SE) (40 ml/daily for 6 months) to the MD. Anthropometric/demographic measures, liver function, metabolic and inflammatory status, flow mediated dilatation (FMD), liver ultrasound and abdominal fat features were analyzed at baseline (TO) and after 6 months (T6).

All patients had good MD (mean Perceived Dietary Adherence Questionnaire = 45, in both groups) and EVOO intake adherence. No differences were found at TO between groups. From TO to T6, a significant (p<0.05) reduction was found in HPPE and SE groups for: waist circumference (WC), glycated hemoglobinemia (HbAIC), visceral fat thickness and FMD. Only HPPE patients had a significant reduction of body mass index (BMI), insulinemia, HOMA-IR, AST and subcutaneous fat thickness. However, when comparing the two groups at T6, no difference was observed, even though a major reduction was shown in the HPPE group for BMI, WC, ALT, HbAIC, triglycerides, total and LDL-cholesterol, subcutaneous and visceral fat thickness.

In conclusion, this preliminary analysis shows that the MD plus EVOO for 6 months can improve metabolic and cardiovascular parameters in MS/MAFLD subjects. No differences at T6 were found between HPPE and SE groups, even though HPPE seems to potentially have more extended efficacy. No effect was proved regarding liver steatosis. Our preliminary data were most likely affected by the low number of patients, and we hope to prove significance while completing the study.

#### Keywords

extra virgin olive oil, metabolic syndrome, metabolic associated fatty liver disease, cardiovascular risk.

#### Funding

This work was supported by the project n. o8TP1041100162 named TRIAL "Code IRIS/U GOV 16463" "PO FESR Sicilia 2014-2020" to LG.

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# Biochemical tools to explore the beneficial effects of phytochemical on human health

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#### Abstract

Inflammation is a beneficial host response to foreign challenges or tissue injury, ultimately leading to the restoration of tissue structure and function. However, if dysregulated, it can play a key role in the onset and/or development of a wide range of pathological conditions, ranging from cancer to neurodegenerative diseases. While the maintenance of physiological levels of oxidants is essential for life processes, a disruption of the endocellular redox homeostasis has consistently been demonstrated to trigger specific signaling events involved in the dysfunctional activation of the immune system.

Nutrition is one of the most important modifiable factors affecting human health. Interestingly, appropriate dietary patterns have been demonstrated to effectively counteract both the onset and the development of redox-dependent, inflammatory conditionsl. Coherently, overwhelming amount of scientific data has demonstrated that dietary phytochemicals can have a positive impact on human health by positively affecting the inflammatory response. First considered 'health-promoting' by virtue of their radical-scavenging activity and/or direct antioxidant effects on cellular biomolecules, such compounds are now believed to interfere with a dysregulated inflammatory response by intercepting reactive species at the level of critical cell signaling pathways.

Within this scenario, biochemical tools to evaluate the redox-modulating and anti-inflammatory potential of phytochemicals appears of particular interest. Moreover, current pharmacological therapies strongly rely on a combo-therapeutical approach. In this regard, the evaluation of synergistic effects of phytochemicals either with drugs or within phytocomplexes, is a crucial aspect to be evaluated and it is increasingly attracting the interest of pharmaceutical and nutraceutical companies. Along these lines, this presentation will cover the most up-to-date, recurrent and acknowledged biochemical strategies to evaluate the anti-oxidative, anti-inflammatory, anti-dysmetabolic and neuroprotective potential of phytochemicals, either alone or in combination.

#### Keywords

phytochemicals, oxidative stress, inflammation, dysmetabolism, neuroprotection.

#### References

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## "Golden" Tomato consumption ameliorates metabolic syndrome: a focus on the redox balance in the high-fat diet- fed rat

Giuditta Gambino 1\*, Giuseppe Giglia 1, Mario Allegra 2,3, Valentina Di Liberto 1, Giuseppe Ferraro 1,2, Pierangelo Sardo 1,2 and Danila Di Majo 1,2

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#### Abstract

Tomato fruits defined as "golden" refer to a food product harvested at an incomplete ripening stage with respect to red tomato at full maturation. The aim of this study is to explore the putative influence of "golden tomato" (GT) on Metabolic Syndrome (MetS), especially focusing on the effects on redox homeostasis. Firstly, the differential chemical properties of GT food matrix were characterized in terms of phytonutrient composition and antioxidant capacities, with respect to red tomato (RT). Later on, we assessed the biochemical, nutraceutical and eventually disease-modifying potential of GT in vivo in the High-Fat Diet rat model of MetS. Our data revealed that GT oral supplementation is able to counterbalance the MetS-induced biometric and metabolic modifications. Noteworthy, this nutritional supplementation proved to reduce plasma oxidant status and improve the endogenous antioxidant barriers, assessed by strong systemic biomarkers. Furthermore, consistently with the reduction of hepatic reactive oxygen and nitrogen species (RONS) levels, treatment with GT markedly reduced the HFD-induced increase in hepatic lipid peroxidation and hepatic steatosis. This research elucidates the importance of food supplementation with GT in the prevention and management of MetS.

#### Funding

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## Astonishing health-promoting properties of Sicilian mango bio-wastes: anti-adipogenic and anti-lipogenic effects of mango extracts on mature 3T3-L1 adipocytes

Giovanni Pratelli 1\*, Antonella D'Anneo 2, Diana Di Liberto 1, Daniela Carlisi 1, Antonietta Notaro 2, Federica Affranchi 2, Giuseppe Calvaruso 2, Marianna Lauricella 1

#### **Abstract**

Obesity is a medical condition characterized by an expansion of white adipose tissue due to increased number of adipocytes (hyperplasia) and/or accumulation of fat in pre-existing adipocytes (hypertrophy). Obesity represents a risk factor for the development of several chronic and deadly diseases, including diabetes, heart disease, and some types of cancer. Inhibition of adipocyte differentiation or reduction of lipid accumulation in adipocytes represents a strategy to combat obesity and related diseases. Mango (Mangifera indica L.) is a plant belonging to the Anacardiaceae family whose cultivation is widespread in tropical and subtropical areas of the world, including different areas of Sicily (Italy). Mango peel and seed are the main bio-waste products from mango processing, representing a consistent part of the fruit. HPLC/Mass characterization of phenolic compounds highlighted that both Mango Peel (MPE) and Mango Seed (MSE) extracts cultivated in Sicily are endowed with a high content of polyphenols with anti- oxidant properties. In our study e demonstrated the ability of MPE and MSE to reduce 3T3-L1 adipocyte differentiation. We also provided evidence that mango extracts reduced lipid accumulation in mature 3T3 adipocytes induced by high levels of the saturated fatty acid palmitate. Mechanistic studies provided evidence that MPE and MSE exerted anti-adipogenic and anti-lipogenic effects by down-regulating the key adipogenic transcription factors PPAR and SREBP as well as activating AMPK. In addition mango extracts exert remarkable anti- inflammatory effects by inducing Nrf2/HO-1/MnSOD pathways. Therefore, our studies suggests a potential use of bio-waste products of mango for counteracting obesity.

#### Keywords

Obesity, Mangifera indica L., bio-wastes.

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# Nutraceuticals for food: a biotechnological opportunity for safety and quality of foodstuffs

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#### Abstract

Heavy metals and metalloids can be highly toxic even in trace elements and are among the most frequent pollutants in sites hosting industrial activities. Most of the chemical substances released into the environment, due to an increasing level of human pollution (air, water and soil), can be found in food products in the form of contaminants. The meaning of contaminant is reported in Reg. (CEE) n. 315/93.

The highest standard of food safety is a strategic priority for the European Union which, starting from the "White Paper on Food Safety" launched by the European Commission in 2000, has consolidated this objective in an articulated way by proposing to address "from farm to fork" all food safety problems that start from primary production and develop up to the consumer's table.

Metals such as arsenic, cadmium, lead and mercury, accidentally present in agri-food production as residual contaminants or process contaminants, are particularly toxic and dangerous (because they easily bioaccumulate) and regulated by Reg. (EC) No. 1881/2006 which fixes the maximum permissible levels in foods. It is true that the presence of metals within the permissible limits in foods, especially in some beverages, represents a problem of a technological nature, i.e. they cause instability over time, reducing their shelf life.

The food quality of some beverage, in fact, is greatly reflected in the stability, which preserves their function and appreciation by the final consumer.

The stability of products such as wine, beer or fruit-based products is often compromised by the presence of residual chemical contaminants such as heavy metals (in concentrations even below the legal limits). Our group is currently carrying out scientific studies for the development of biotechnological systems, which not only have health properties for the final consumer (nutraceuticals) but above all which have a chelating and/or demetallizing action, also which are non-toxic and biocompatible, starting from microbiological matrices and/or in combination with vegetable extracts, capable of reducing the concentrations of heavy metals in lightly processed drinks, to ensure the maintenance of the qualitative characteristics of the food products and above all the safety of the final consumer.

#### Keywords

Heavy metals, food safety, food quality, food demetallization, biotechnological systems, inorganic contaminants.

#### Funding

This work is part of the PhD in "Biodiversity in Agriculture and Forestry", (XXXVIII cycle), University of Palermo.

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# Bioactive compounds from in vitro hop plants: from synthesis factors to practical applications

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#### Abstract

Natural products, derived from an increasing range of medicinal plants, are drawing the attention of an everyday wider portion of enterprises, interested in place on the market plant-based additives to be used in agri-food, pharmaceutical and cosmetic sectors. Hop (Humulus lupulus L.) is wealth in bioactive compounds which have antioxidant, antimicrobial and, antiviral properties: terpenoids, phenolic compounds (i.e. xanthohumol); alkaloids; bitter acids (humulone and lupulone). (Nionelli et al 2018). These secondary metabolites with biological activity are present in the whole hop plant, not only in the cones used, mainly, for beer production, but also in vegetative biomass (Ceh et al 2007). Exploiting the hop vegetative biomass, usually considered a waste, for extracting bioactive compounds, could represent a way to make hop culture less impacting, and to guarantee a secondary income for growers. It has been proved that vitro-derived hop plantlets produce the same secondary metabolites as the in-field grown plants; thus, this plant material can be used to provide a standardized ,matrix homogeneous and independent of the environmental conditions (Scarpa et al 2022). In this research the total polyphenol content, the antioxidant and antimicrobial activity of extracts obtained from leaves and stems of plants grown in open field, and leaves and roots from vitro-derived hop plantlets were studied, , in order to characterize the vegetative biomass of hop and to, further, evaluate the possibility of using the obtained extracts in the food and non-food sector. Results obtained are really encouraging, evidencing that both leaves from in field and in vitro grown plants are a rich source of bioactive compounds, and that the most representative hop compounds are present in both matrices. This study represents a starting point for more deep investigation and for the evaluation of future application of the hop extracts.

#### Keywords

Bioactive compounds, chemical characterization, Humulus Lupus L., plant tissue culture

#### Funding

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### Probiotic as future functional food in aquaculture

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#### Abstract

In accordance with the international trajectory of blue growth, circular economy and one health approach to the aquaculture sustainable research theme and through research dedicated to the development of Integrated Multitrophic Aquaculture Systems, one experimental feed study on the commercial sea bream (Sparus aurata L) has been carried out. Sparus aurata samples used to experimental study has been transferred to the IRBIM-CNR facility (Messina, Italy) and reared in fibreglass tanks where the primary water parameters (Temperature, O2, and pH) were controlled with a multi-parameter probe, (YSI Professional Plus Multi-Parameters). The fish were fed with 3 diets, including two probiotic and one standard as control.1 In order to determine the health of the fish, two samplings were carried out during the rearing period: the first when the fish have reached a weight of about 90g, while the second when the fish have reached the marketable size (about 350g). At the conclusion of each period, the animals were sacrificed, and a nutraceutical analysis was conducted (under the supervision of the IRBIM-CNR facility of Mazara del Vallo) to assess the quality of the fish reared with the three diets.

Additionally, as part of this project, the physiological role of an animal's ability to adapt to its microbiome's gut environment as a result of different feeding practises was taken into consideration. Blood parameters2, as well as the metabolism of both amino acids and energy, were studied3.

In order to ensure consistency with the experimental data on probiotic diets, all analyses were ultimately repeated on sea bream samples as well. Additional comparative studies of wild and sea bream were also conducted.

#### Keywords

functional food, Sparus aurata, Animal Helth

Funding: This study is part of Horizon 2020 EU project "Controlling mlcRobiomes CircuLations for better food Systems" (CIRCLES") which aims to develop and translate innovative tailor-made circular actions dedicated to the microbiome into concrete applications to improve the main supply chains of the EU food system and their overall sustainability.

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### Spray-dried 'green' polyphenols-enriched extracts from waste bentonite to produce nutraceuticals for oral care

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#### Abstract

The term 'nutraceuticals' is widely used to intend natural bioactive compounds having characteristics similar to nutrients and pharmaceuticals. Lipids, vitamins, carbohydrates, proteins, minerals, and other molecules (e.g., polyphenols) are considered nutraceuticals as they have both nutritional roles as well as health-promoting, disease-curing, and preventive activities. A long-term intake of polyphenols, as well as their topical application, has been proven to prevent several diseases due to their wide range of beneficial properties (e.g., antioxidant, anti-inflammatory, antimicrobic) [1,2]. Polyphenols are naturally occurring in fruits, vegetables, and plants and can also be found into such agri-food wastes. In an ever-grown perspective of circular economy, the identification of novel wastes to be valorised as source of functional biomolecules could be a virtuous 'green' approach. Focusing on the grape processing industry, steam, peel, and lees have already been valorised, while the bentonite is till now considered just an abundant waste (100 g of bentonite to clarify 1 hL of must/wine) [3]. The aim of our work is to recycle the waste black bentonite (bentonite:activated carbon=1:1), the most popular fining agent, by extracting the polyphenolic pool in it entrapped. In view of a waste-to-market approach, PEG200 and Propylene Glycol were chosen as unconventional solvents due to their safety, eco-friendliness as well as widespread use in the pharmaceutical and cosmetic fields. The polyphenols-enriched colored liquid extracts were obtained by maceration, recovered by centrifugation, and characterized in terms of antioxidant and scavenger properties (DPPH assay), total phenolic and protein contents (HPLC-DAD, Folin-Ciocalteu and Bradford assays), safety (eye and skin irritation/sensitization) and stability (six-months storage). As a result, they can be considered precious functional secondary raw materials. The best extract was thus used to design nutraceutical products for oral care purposes. By spray drying, a fine, reproducible, and easy workable matrix powder was obtained, consisting in homogeneous polymeric microparticles made by the novel value-added 'green' extract together with other selected excipients (polymer, sweetener, penetration enhancer). The so-obtained powder was then directly compressed to produce orodispersible buccal tablets. These could represent a friendly nutraceutical product to locoregionally prevent or treat several oral diseases such as mouth sores, infections, and mucositis.

#### Keywords

Polyphenols; Agri-food waste recovery; Green extraction; Spray Drying; Oromucosal tablet

#### Funding

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# Hydro-alcoholic and supercritical fluid preparations from Sicilian grape pomace induce apoptotic cell death in HCT116 colon cancer cells

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#### Abstract

In the last years the interest in the use of phytocompounds has grown considerably. Bioactive molecules derived from plants and vegetables were recognized having a beneficial effect on human health, exerting different biological activities. Natural compounds are able to neutralize the reactive oxygen species, to modulate detoxifying enzymes, to counteract the effects of cellular aging, to act as anti-inflammatory and, potentially, they are able to assist the best known synthetic molecules in the prevention of cancer.

Since significant amounts of bioactive molecules are still disposable in agri-food waste, we are interested to investigate the health potential of Sicilian vinification by-products, such as grape pomace.

The biological activity of grape pomace extracts obtained through two different methods, a traditional hydro-alcoholic and an innovative method based on the use of supercritical fluid extraction, was evaluated on HCT116 colon cancer cells. In this preliminary study, we observed a greater reduction of cell viability after treatment with Supercritical Fluid Extract (SFE) then Hydro- alcoholic (HE) one. Indeed, we obtained the same viability reduction (about -70%) employing much lower concentration of SFE than HE. Nevertheless, SFE and HE seem to activate the same molecular pathway involving the activation of caspase-3 and PARP cleavage. These events, probably, were related to an apoptotic response of the cells. In addition, Hoechst staining showed DNA condensation and fragmentation thus confirming the induction of apoptosis.

It is still a preliminary study, next step will be to better understand the key players of the apoptotic pathway and to characterize phytochemical composition of the extracts using HPLC/MS.

#### Keywords

grape pomace by-products, cancer cells, antitumor effects, apoptosis induction.

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### Assessment of cellular safety of Sicilian Brassica extracts

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#### Abstract

Growing evidence highlights the importance of edible plants as source of health-promoting compounds. Sicily, home of biodiversity, counts different endemic species spontaneously growing, as the Brassicaceae family, traditionally consumed in the human diet and extensively used in traditional medicine from ancient times. We focused our attention on the genus Brassica, including in Sicily ten endemic species, with recognized nutritional proprieties and sources of several bioactive compounds, such as carotenoids, tocopherols, ascorbic acid, glucosinolates. Due to the importance of exploring medicinal plants for their efficacy but also for safety and toxicity, at first we aimed to test and compare in vitro the cytotoxic effects of extracts of flowers, fruits and leaves from three endemic Sicilian Brassica, taking into account that geographical factors can influence the chemical composition and the biological activity of the plants.

From February to May B. tardarae, B. rupestris ssp hispida, B. macrocarpa were collected in their endemic locus ("Gole della Tardara", Ficuzza and Favignana island respectively). Samples of flowers, leaves and fruits from each plant were separated and air-drying was performed at a constant temperature of 20°C in a dark place, to preserve the bioactive molecules from degradation. After 15 days, they were powdered for extraction with methanol. The cytotoxic effects of flower, leaves and fruits of Brassica extracts were evaluated by Trypan blue assay, using differentiated Caco-2 cells were exposed to increasing concentrations of extracts (from 0.05 to 1 mg/mL) and after 24 h cell viability was calculated and compared to untreated cells, taking as control.

No toxicity was observed at all concentrations tested for each extracts, being the cell viability, at the highest concentrations tested, up to 72%, 80 % and 76% respectively for leaves, flowers or fruits. No significant differences were observed among the three Brassicae (P>0.05).

Our data suggest the safety of the extracts from the Sicilian Brassicae analysed. These data encourage further studies to evaluate the potential use of Sicilian Brassicae as candidates for drug formulation for human health.

#### Keywords

Sicilian Brassica, bioactive compounds, cytotoxicity, human health.

### Ginger extraction and characterization: gene expression analysis of anti-inflammatory and antioxidant effects

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#### Abstract

The rhizome of Zingiber officinale Roscoe (ginger) is commonly consumed as a spice, and has long been used as an herbal medicine with anti-inflammatory, antioxidant and anticancer properties. It is composed of many bioactive constituents, mainly gingerols and shogaols (Mao et al 2019). Although the bioactive compounds have been identified, to date the molecular mechanisms of ginger action and the related signaling pathways are still partially defined. In this study, we used a simple ethanol and freeze-drying method to extract ginger compounds. The total ginger extract (GE) was chemically characterized by HPLC and antioxidant tests (Folin-Ciocalteu and ORAC tests). The anti-inflammatory/antioxidant effects of GE, and of commercial [6]-gingerol, were evaluated on RAW 264.7 murine macrophage cells. Cells viability tests confirmed which doses of GE and [6]-gingerol were not toxic for cells. We analyzed the antioxidant property of GE at the cellular level using the glutathione (GSH) assay on cells treated with LPS and pre-treated or not with GE. We found that GE significantly increased the GSH/GSSG ratio, as well as rescued the reduction caused by the LPS treatment, confirming its antioxidant activity. By quantitative PCR, we analyzed the differential expression of different categories of genes (signaling, pro- and anti-inflammatory cytokines, enzymes, macrophage specific and endoplasmic reticulum stress response genes) in cells treated with LPS for 24h, after a 2h pre-treatment with GE, using untreated cells as controls. The results showed that GE pre-treatment of cells reduced the LPS-induced expression of TLR4 and MYD88 genes (signaling pathway), as well as of IL-1 , IL-6, IL-10, TNF- (cytokines). It also reduced iNOS and TRIB3 expression, whereas increased the expression of HO-1 and Arg-1 genes. No effects on the expression of Light/Tnfsf and MIF (macrophage specific) genes was found. The pre-treatment with [6]-gingerol alone had similar effects. These results altogether showed that GE pre-treatment is able to promote a specific polarization of macrophages, which switch from pro-inflammatory M1 versus anti-inflammatory M2a/M2c phenotypes.

Further analyses are needed to better understand the role of the single components of GE on inflammation. An interesting study would be to evaluate the ginger bioavailability in the human body.

#### Keywords

gene expression, inflammation, toxicity, bioactive molecules, cytokines.

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# Bioactive phycocyanin recovery – an innovative approach to get concentrated blue pigment of high purity grade

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#### Abstract

Phycocyanin is a water soluble, brilliant blue and highly fluorescent pigment-protein of the photosynthetic light-harvesting antenna complexes in, mainly, cyanobacteria, Rhodophyta and Cryptomonads. It is one of the few natural blue pigments available as food colourant, but it is also a safe bioactive compound having antioxidant, anti-inflammatory, anticancer, antiviral, immunity-boosting and other therapeutic activities. Phycocyanin has many biotechnological applications in food, cosmetic, pharmaceutical and medical sectors, as functional food, colorant, fluorescent tag, drug, photosensitizer in cancer photodynamic therapy.

We have developed an innovative two-step extraction process to obtain bright blue phycocyanin crude extracts with high purity grade P (within 2.5 and 3.5) directly from fresh biomass of Arthrospira platensis Gomont 1892 (commonly named Spirulina). We found out and for the first time exploited ammonium sulphate capability to minimize the release of water soluble phycobiliproteins in aqueous medium during ultrasound-assisted cell lysis/purification phase. The conventional sequence which is, extraction followed by purification, was reversed. The extraction phase was decoupled from biomass cell lysis. Cell lysis, accomplished by ultrasonication in ammonium sulphate solution, was merged with purification in a single step, before the pigment extraction/recovering phase. The process was entirely carried out in aqueous solutions. No downstream purification was required to obtain products suitable for the most common phycocyanin applications (i.e. foods, nutraceuticals and cosmetics). Production time, hours instead of days, was reduced to the advantage of the product quality. The process benefits are: (1) direct use of extracting solutions that cannot be used in the ordinary ultrasound-assisted extraction of phycocyanin (because of the extensive simultaneous extraction of contaminant molecules), (2) gain of high commercial value phycocyanin due to the elevated purity grade and (3) direct production of highly concentrated bright blue pigment crude extracts (up to about 5 mg mL-1) immediately in hand to the market.

#### Keywords

Phycocyanin extraction; Ultrasonication; Ammonium sulphate; Arthrospira platensis; Market benefits, Nutraceuticals

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# The hydroxytyrosol induces the apoptotic cell death of human melanoma cells

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#### Abstract

Melanoma is one of the most aggressive cancers worldwide and the deadliest form of skin cancer whose incidence rate, unfortunately, is increasing rapidly in western populations. Indeed, metastatic melanoma is one of the most drug-resistant cancer that often acquires the capacity to evade the cytotoxic action of therapeutic options inducing the breakdown of cell death control. Therefore, in the aim to identify new potential therapeutic drugs suitable to overcome the intrinsic survival features acquired by melanoma cells, we studied the role of hydroxytyrosol [2-(3,4-dihydroxyphenyl) ethanol or 3-hydroxytyrosol], the major phenolic component of olive oil (1), on the inhibition of human melanoma cell growth and survival. Interestingly, olives and olive oil are crucial components of the Mediterranean diet and their regular intake has been related to reduced risk of several chronic diseases such as cancer (2). Therefore, we improved and increased this field of research analysing in metastatic melanoma cell lines, the anti-proliferative and pro-apoptotic potentials of the hydroxytyrosol (3). In particular, through MTS assay, DeadEnd™ Colorimetric TUNEL assay, Annexin V binding and PI uptake, western blot experiment, intracellular reactive oxygen species (ROS) analysis and the cell colony assay, we showed that the hydroxytyrosol treatment remarkably reduces the cell viability inducing the death for apoptosis of melanoma cells. Moreover, we showed that the hydroxytyrosol treatment of melanoma cells leads to a significant increase of p53 and H2AX expression, a significant decrease of AKT expression and the inhibition of cell colony formation ability. Finally, we propose that the increased amount of intracellular reactive oxygen species (ROS) that may be related to the regulation of the pathways involved in the activation of apoptosis and in the inhibition of melanoma growth, could be the strategy used by hydroxytyrosol to exert its functions in melanoma. Indeed, hydroxytyrosol is widely accepted in cancer treatment for its anti-tumour properties and low toxicity, therefore, for its role in melanoma growth inhibition, the hydroxytyrosol treatment could deeply interfere with melanoma progression as a promising therapeutic option for the treatment of this highly invasive tumour.

#### Keywords

Melanoma; hydroxytyrosol; cellular growth; apoptosis; ROS

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### Active biomolecules from microalgae in IBD treatment

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#### Abstract

Inflammatory bowel disease (IBD) is a multifactorial idiopathic chronic inflammatory condition affecting the gut. Animal models are indispensable to study various aspect of IBD and to facilitate preclinical drug/therapy design to target specific components involved in IBD pathogenesis. Rodent model of colitis induced by intrarectal injection of 2,4 dinitrobenzensulfonic acid (DNBS), results in colon inflammation and ulceration similar to Crohn's disease patients and is widely used to study potential role of nutraceuticals in IBD therapy. Using DNBS rat, we studied possible beneficial effects of treatment with the blue-green algae Aphanizomenon flos aquae (AFA), rich in bioactive products, to prevent colonic inflammation. In our study AphaMax® an aqueous AFA extract, kindly supplied by Nutrigea Research s.r.l., rich in phycocyanins and phytochrome, (20,50 or 100 mg/kg/day) was administered for 14 starting 7 days before the day of the colitis induction. Body weight loss, stool consistency, rectal bleeding, colon weight/length, histopathology, myeloperoxidase activity (MPO), inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) expression and pro-inflammatory cytokine levels were assessed. Evaluation of nuclear factor- B (NF- B) p65 protein levels and detection of oxidative and nitrosative stress markers were also performed. AphaMax® treatment significantly attenuated the severity of DNBS-induced colitis, as evidenced by less severe clinical signs (body weight loss diarrhea incidence, rectal bleeding), decreased of colon weight/length ratio, attenuation of the macroscopic and histological colonic damage and of the neutrophil infiltration. Aphamax treatment also reduced the levels of proinflammatory cytokines and down-regulated the expression of NF- B p65, as well as the expression of the inducible proteins iNOS and COX-2 and the levels of reactive oxygen species and nitrite. Our results indicate the AphaMax® supplementation is able to reduce colon injury induced by DNBS in rats, mainly due to its anti-inflammatory and anti-oxidant effects, suggesting that AphaMax® could be a good candidate as a complementary drug in the treatment of IBD.

#### Keywords

AphaMax®, microalgae, inflammatory bowel disease (IBD), Aphanizomenon flos-aquae (AFA), colon, antioxidant

### Formulation strategies for a successful food supplements

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#### Abstract

The growing demand of food supplements must not underestimate the concept of quality (as safety and efficacy); quality is the only most effective tool for promoting and making finished products really competitive, safe and effective. Quality is a concept that must be pursued and built from the early stages of product development, up to its production and distribution.

Scientific criteria (the correct amount of the active ingredients defined through scientific studies), regulatory criteria (inform clearly and exhaustively the content and the benefits of the active ingredients) and technological criteria (the definition of the ideal pharmaceutical form that allows the release of the active ingredients in the correct site) are fundamental parameters to obtain those goals.

In order to present one example of scientific study, some results were shown: some mice were treated with a high-fatty diet to induce non-alcoholic fatty liver disease (NAFLD) and to evaluate whether the co-administration of a supplement (containing Curcumin, Silymarin, Guggul, Chlorogenic Acid and Inulin) could protect the liver from the induced damage. the supplement proved capable of limiting liver damage as shown through morphological, histological, blood and genic evaluations (1).

Keywords Quality, Food supplements, Efficacy

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# Funding Research & Innovation Projects: previous experiences and opportunities

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1 M&D

#### Abstract

Funding opportunities for Research Development &Innovation (RD&I) projects has never been such consistent and various as in this EU Coesion Policy Program period (2021-2007). Direct and indirect grants are guaranteed to SMEs and big firms, standing alone or involved in cooperation projects with public or private research centres. One of the most important Policy Objective of programming period 2021 – 2027 is PO 1, "a more competitive and smarter Europe by promoting innovative and smart economic transformation and regional ICT connectivity" and even the other OPs should be pursued taking in deep consideration RD&I project results. A case study of RD&I projects taken by ongoing programming period will be examined.

Keywords EU, Grants, Research, Development, Innovation

### Beer Attenuates Diet-Induced Obesity and Hepatic Steatosis in Mice

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#### Abstract

Beer is a fermented beverage widely consumed worldwide, rich in chemical compounds of natural origin with high nutritional and biological value. It is made up of water, barley malt, hops, and yeast. The main nutrients are carbohydrates, amino acids, minerals, vitamins, and other compounds such as polyphenols which are responsible for the many health benefits associated with the consumption of this drink (1). Hops and malt are one of the raw materials for beer and are a source of phenolic compounds. In fact, about 30% of the polyphenols in beer are to be attributed to hops and 70%-80% to malt (2). Flavonoids belong to the polyphenol family and represent a key molecular component of plant-based diets because of their antioxidant, antiobesogenic, and chemoprotective properties by scavenging free radicals and activating molecular effectors implicated in human disease (3). The present study aimed to characterize the phenolics content of beer and investigate whether it prevents high-fat diet (HFD)-induced obesity and steatosis in mice. Beer was characterized for total phenols, flavonoids and flavonols. Male C57BL/6 mice were divided into four groups: 1) Control (C), 2) High fat diet (H), 3) Control plus 0.23% Beer (CBr) and 4) High fat diet plus 0.23% Beer (HBr) for 10 weeks. A good amount of total phenols (25.01 1.27 GAE/100 ml), flavonoids (3.17 0.17 mg CE/100 ml) and flavonols (3.07 0.23 mg QE/100 ml) was found in beer. The administration of beer to dislipidemic mice significantly decreased the AST (151.40 51.40 U/l vs 301.25 70.02 U/l, p<0.05) and ALT (37.20 4.17 U/l vs 66.50 10.11 U/l, p<0.001) values in comparison to HFD-fed mice, but did not affect blood biochemical parameters (total cholesterol, low-density lipoprotein cholesterol and glucose). Moreover, HBr-treated mice showed a significant reduction of final body weight (36.27 2.77 g vs 40.90 4.55 g, p<0.01) and hepatic lipids level (43.92 18.76 mg/g vs 78.20 7.51 mg/g, p<0.01), as compared to HFD-fed mice. These preliminary results suggest that beer is reach in phenolic compounds that may contribute to exert beneficial effects against obesity and steatosis of HFD-fed mice.

#### Keywords

Non-alcoholic fatty liver disease (NAFLD), weight gain, beer polyphenols

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#### Tritordeum as a nutritional alternative to wheat

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#### Abstract

Tritordeum is a cereal species that resulted from the hybridization between durum wheat (T. durum) and wild barley (H. chilense). It is considered a natural crop since obtained using traditional breeding techniques.

In this study, Tritordeum was explored as a candidate for low-toxic cereal species. Two registered varieties, Bulel and Aucan, were selected and the biological effects of their prolamin-digested samples (DPs) were evaluated in vitro by mimicking the gastrointestinal digestion process. T. aestivum (Mieti), and T. durum (Provental) were employed as controls. Extracted prolamins were digested by gastric and pancreatic proteases and the biological effects of DPs were determined on Caco-2 differentiated on transwell inserts [1]. Changes in cell viability, monolayer permeability, organization of F-actin microfilaments, and ER stress, triggered by DPs were explored [2].

Exposure to Mieti- or Provental-DP readily disrupted the tight junction barrier. Interestingly, Aucan-DP induced no change in monolayer permeability, whereas Bulel-DP exerted only slight effects. The toxicity of Mieti- and Provental-DP was confirmed by analysing the changes induced in the organisation of the cytoskeleton of enterocytes and cell viability. In contrast, Aucan-DP and Bulel-DP induced no negative effects on either monolayer viability or cytoskeleton organisation.

Proteomic analysis showed that DPs profiles of Tritordeum lines were sufficiently different from controls to determine lower toxicity. Concerning carotenoids, lutein, violaxanthin, cryptoxanthin, zeaxanthin and -carotene were also quantified with low levels in T. aestivum. As expected, the content of free carotenoids was higher in both Tritordeum lines than in the wheat species; lutein was the main carotenoid compound found in both Tritordeum and Triticum genotypes. The results support the use of both Tritordeum lines as interesting candidates for the development of nutritional approaches to reduce the toxicity of wheat flour. In addition to nutritional considerations, higher levels of carotenoids are an important characteristic of wheat flour for baking.

#### Keywords

Tritordeum, low-toxic cereal, gastrointestinal digestion

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# High amylose wheat phenolic extract attenuates vascular inflammation in a co-culture model of intestinal epithelial and endothelial cells

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#### Abstract

Whole wheat is a rich source of various phytochemicals with health-promoting properties. Consumption of foods made from whole wheat has been associated with a lower risk of cardiovascular disease (1). Newly developed high-amylose durum wheat (cv Svevo), characterized by a high content of resistant starch and phenolic acids, including ferulic acid and sinapic acid, is gaining interest as a healthy ingredient for functional food (2). The aim of the present study was to investigate the effects of the intestinal metabolites of high amylose wheat phenolic extracts (WPE) on vascular inflammation. We established a transwell epithelial-endothelial co-culture system with Caco-2 cells mimicking the intestinal layer and HMEC-1 as endothelial cells mimicking the vascular layer (3). Caco-2 cells were grown on semipermeable filters for 21 days to differentiate and develop an enterocyte-like phenotype. Then, Caco-2 cells were moved to 6- or 12-well plates, containing HMEC-1 cells in the lower compartment. WPE (1, 5, and 10 µg/mL gallic acid equivalents) was added on the apical compartment for 2 h. Afterwards, TNF (10 ng/mL) was applied on the basolateral compartment for 16 h to simulate the inflammatory milieu. Thereafter, the integrity of Caco-2 monolayers was assessed with the luciferase yellow assay. In HMEC-1 cells, endothelial-leukocyte adhesion, as well as the expression of endothelial inflammatory mediators (cell adhesion molecules, cytokines and chemokines), intracellular reactive oxygen species (ROS) levels and NF-kB activation were evaluated by multiple assays.

The results showed that trans-epithelial WPE suppressed, dose-dependently, the endothelial expression and release of interleukin (IL)-6, monocyte chemoattractant protein (MCP)-1, as well as, the expression of endothelial adhesion molecules, such as intercellular adhesion molecule (ICAM)-1 and vascular cell adhesion molecule (VCAM)-1, and inhibited the subsequent adhesion of leukocytes to endothelial cells under pro-inflammatory conditions. The anti-inflammatory effect of trans-epithelial WPE on endothelium was mediated by inhibition of NF-kB activity and reduction of intracellular ROS levels.

In conclusion, the intestinal metabolites of the phenolic components of high amylose wheat were able to reduce vascular inflammation, suggesting high amylose durum wheat as an excellent functional food ingredient for cardiovascular disease prevention.

#### Keywords

Vascular inflammation, metabolites, phenolic acids, whole wheat, gene expression, antioxidants

#### Funding

This research was partially supported by PRIMA Section 1 2020 Agrofood Value ChainIA Topic: 1.3.1-2020 (IA), MEDWHEALTH, project grant no. 2034

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### Red grape pomace functional beverages dampen intestinal epithelial cell inflammatory response

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#### Abstract

Grape pomace is a rich source of nutraceutical compounds with multiple bioactivities that could be exploited to prevent chronic inflammatory diseases. Our research group has previously found that polyphenols from red grape skins mitigated the excessive inflammatory response in leukocytes and vascular endothelial cells by reducing intracellular oxidative stress (1-3). However, the role of red grape pomace as a natural and safe source of polyphenols on gut inflammation, which is a defining feature of inflammatory bowel diseases, such as Crohn's disease and ulcerative colitis, is unknown. The aim of our research activity was to obtain and characterize grape pomace-derived functional beverages for preventing gut inflammatory diseases. To this purpose, we investigated whether red grape pomace polyphenol extract (GPPE) was able to attenuate the overwhelming inflammatory response in enterocyte-like cells. The grape pomace substrates were structurally characterised and the stability and safety of the bioactive constituents were evaluated. The nutraceutical properties of our samples were verified by analysing the anti-inflammatory properties in human intestinal epithelial cells (Caco-2), investigating underlying molecular mechanisms. Intestinal epithelial Caco-2 cells, grown in monolayers, were treated with different concentrations of GPPE (1, 5, 10 µg/mL gallic acid equivalents) for 2 h and then stimulated with lipopolysaccharide (LPS) and tumor necrosis factor (TNF) for 16 h. Through multiple assays, the expression of intestinal inflammatory mediators, intracellular reactive oxygen species (ROS) levels and NF-kB activation, were evaluated. The results showed that GPPE supplementation prevented, in a concentration-dependent manner, the intestinal expression and release of cytokines (IL-1beta, TNF, IL-6), chemoattractants (MCP-1 and CXCL-10), other pro-inflammatory markers, including ICAM-1 and COX-2, and matrix metalloproteinases (MMP)-9 and MMP-2. The analysis of the molecular mechanisms highlighted that GPPE anti-inflammatory effect was mediated by the inhibition of NF-kB activity and reduced intracellular ROS levels.

In conclusion, our findings suggest grape pomace as a natural source of polyphenols with health-promoting properties that could alleviate gut chronic inflammatory diseases. By-products of the red wine industry as raw materials, should be valued as part of an environmentally sustainable, innovative process and the associated functional ingredients should be valorised for their health-promoting activities.

#### Keywords

gut inflammation; pro-inflammatory markers; grape pomace; polyphenols; oxidative stress; gene expression

#### Funding

This research was partially supported by the National Recovery and Resilience Plan (NRRP), Mission 4 Component 2 Investment 1.3 – Next-GenerationEU, Project "ON Foods" Project code PEooooooo3, Concession Decree No. 1550 of 11 October 2022; Agritech National Research Center and received funding from the European Union Next-GenerationEU National Recovery and Resilience Plan (NRRP), Mission 4 Component 2, Investment 1.4 – D.D. 1032 17/66/2022, CN00000022).

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### Quercetin as anticalcific agent in vascular disease

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#### Abstract

Vascular calcifications (VC) are characterized by abnormal mineral depositions in the vessel wall and are frequently associated with specific diseases such as atherosclerosis, chronic kidney disease (CKD), and diabetes [1,2]. No specific medical treatments are available in clinical practice; in terms of prevention, some natural compounds assumed through the diet or by integration with natural bioproducts, like Curcumin, Resveratrol, and Magnesium, have shown, in literature, the potential to inhibit the disease process in experimental models [3]. In addition to the specific evaluation of compounds on vascular cells and considering the peculiar environment where vascular cells live, continuously exposed to blood flow, a valuable approach for a more realistic and effective analysis is represented by in-vitro dynamic cell model systems that recapitulate the hemodynamic environment. In this work, we focused on the effects of Quercetin on a dynamic culture (250 l/min flow rate) of Human Coronary Artery Smooth Muscle Cells (HCASMCs) using a double-flow bioreactor (LiveBox2, IVTech Srl, Massarosa, Italy). Our aim was to evaluate the anti-calcific (quantifying intracellular Ca2+) and anti-inflammatory (quantifying Interleukin 6 (IL-6)) effects of Quercetin, which, among the other natural compounds tested, resulted in the more interesting. HCASMCs were treated with a DMEM High Glucose supplemented with 1,9 mM phosphates solution (NaH2PO4/Na2HPO4) in the presence or absence of Quercetin 100 M for 7 days. At the end of the experiment, cells and media samples were collected. Intracellular Ca2+ and IL-6 resulted significantly decreased in HCASMCs cultured under calcifying conditions and treated with Quercetin for 7 days.

These preliminary analyses highlighted the potential beneficial effect of a preventive assumption of Quercetin to contrast the calcific processes at vascular levels.

#### Keywords

HCASMC, Ouercetin, Calcification, Inflammation

#### Funding

This work was supported by SOFIA Project Co-Funded by Regione Toscana within Programma operativo regionale (Por) Fondo europeo di sviluppo regionale (Fesr) 2014-2020 - Bando 2: Progetti di ricerca e sviluppo delle MPMI.

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### Nutraceuticals in the prevention of viral Infections

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#### Abstract

Recently, scientific interest was focused on nutraceuticals, which are those biomolecules in foods or vegetables that have beneficial effects on health. The pharmacological properties of natural biomolecules have gained increasing attention in the field of alternative and coadjutant therapeutic approaches to infectious diseases (1). These compounds are characterized by negligible side effects in comparison with traditional pharmacological therapies.

During the pandemic of SARS-CoV-2 attention to the antiviral properties of nutraceuticals was increased. It is well-known that polyphenols from fruit and vegetables, biologically active and useful substances have been recognized for their functional importance as antimicrobial, antioxidant, and anti-inflammatory agents and for their ACE-inhibitory activity. In addition, many nutrients, such as vitamins link A, B, C, and D, and minerals like zinc and selenium play an important role in maintaining a healthy immune system. The use of a plant-based diet and appropriate food supplementation could help in reducing the symptoms related to viral infection (2). Thus, developing advanced nutraceutical formulations able to efficacy contrast inflammation, and oxidative stress during infection could prevent complications. To investigate the role of natural compounds in reducing oxidative stress and inflammation some biomolecules from saffron have been extracted and characterized. Picrocrocin, 4-OH safranal, and safranal have been identified as bioactive compounds in the saffron extract. These molecules have evaluated for their anti-inflammatory proprieties. In addition, Caffeic acid, Siringic acid, Gallic acid, and Rosmarinic acid have been selected as potential candidates.

#### Keywords

Biomolecules, nutraceuticals, antimicrobial, antioxidant, anti-inflammatory

#### Funding

This research was supported by "One Health Basic and Translational Research Actions addressing Unmet Needs on Emerging Infectious Diseases PE00000007" project, funded under the National Recovery and Resilience Plan, Mission 4 Education and Research - Component 2 From research to business - Investment 1.3, "Partenariati estesi alle università, ai centri di ricerca, alle aziende per il finanziamento di progetti di ricerca di base" funded by the European Union - NextGenerationEU" - D.D. MUR of concession Prot.n. 0001554 of 11/10/2022.Next

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# Technology Transfer Tools of the National Research Council of Italy (CNR) and Italian Union of Chambers of Commerce (Unioncamere)

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#### Abstract

The PROMO-TT Instrument is a joint project developed by National Research Council of Italy (CNR) and Italian Union of Chambers of Commerce (Unioncamere) for the promotion of CNR technologies to the Productive World, in collaboration with the Chambers of Commerce and with all the relevant Stakeholders (https://promott.cnr.it/it).

The main aims of the PROMO-TT Instrument are:

- a. To create new partnerships at different levels between Researcher Teams, Enterprises, Investors and No-Profit Organizations;
- b. To systemize a shared methodology focused on a better exploitation of the results of research carried out at the National Research Council of Italy;
- c. To accelerate the entry on the market of new technologies;
- d. to promote the creation of new high-tech companies (start-up and spin-off).

Within the frame of the PROMO-TT instrument, an additional tool is represented by the establishment of a Strategic Table on Nutraceuticals and Functional Foods. This Open Structure lead by IRIB-CNR will analyze the needs of the local territorial production making proposals for specific activities interest of the territory (event days; encounters between the world of production and research; training and information, etc).

# Use of ancient wheat crops for the dietary management of patients with wheat-related disorders

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#### Abstract

Gluten, and other wheat proteins including amylase trypsin inhibitors (ATIs) and fermentable short-chain carbohydrates (FODMAPs), have been identified as possible factors for the generation of intestinal and extra-intestinal symptoms in subjects suffering from wheat-related disorders, such as non-celiac wheat sensitivity (NCWS) or irritable bowel syndrome (IBS)

In particular, it is well-known that gluten and ATIs possess immune stimulating activity.

Dietary exposure to the combination of gluten and ATIs exacerbates intestinal immune dysregulation, and increase risk to develop wheat-related disorders.

Triticum monococcum, one of the oldest and primitive cultivated wheat, unexposed to genetic improvements, has been suggested to possibly exert a reduced immunostimulating activity compared to common wheats and, consequently, has been identified as a fitting candidate to be introduced into the diet of NCWS and IBS patients.

We have demonstrated that almost all immunotoxic gluten peptides for Celiac Disease (CD), from two monococcum cvs, Monlis and Norberto-ID33, are degraded by an in vitro gastric-duodenal digestion, whereas gluten immunogenic peptides from common wheats resist intestinal digestion [1]. Moreover, we have shown that ATIs from T. monococcum are degraded during digestion by gastric-duodenal enzymes, compared to ATIs from common wheat and that such susceptibility, resulted in a failure to induce the mucosal immune response in CD.

It should be noted that these studies concern only CD, and that the internationally accepted guidelines currently provide that these patients should, however, avoid any type of wheat or cereal containing gluten, including T. monococcum. Nevertheless, results reported from multiple studies, including our, are encouraging findings that suggest a potential tolerability of T. monococcum for NCWS or IBS subjects.

Moreover, health-promoting properties of ancient wheat have been credited to its superior levels of phytochemicals and phenolic compounds compared with the modern wheat species, suggesting its potentiality as functional foods and nutraceutical ingredients (3).

#### Keywords

Triticum monococcum; wheat-related disorders; Celiac Disease

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# Hemp flour, from waste to nutritional and nutraceuticals reuse

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One of the main objectives of recent years is to characterize and valorize by-products of agri-food industries, as new sources of bioactive components, from the perspective of a circular economy and a biorefinery approach both for environmental and economic reasons.

Hemp flour, obtained from Cannabis sativa seeds, is an example of promising bio-sustainability raw material with a high nutritional value that can be obtained from industrial by-products.

From C. sativa seeds is obtained an oil rich in fatty acids, mainly linoleic and -linolenic acids [1]. After oil extraction, seeds can be ground to obtain edible flour. Foods fortified with these "non-wheat flours" would have an additional supply of fiber, minerals, proteins, and polyphenols, thus increasing the final product's nutritional and beneficial properties.

The objective of this work was to study chemical qualities (polyphenolic profile, amino acids, total phenolic content (TPC), antiradical capacity and fatty acids) of hemp flour, for the possible preparation of functional foods.

The phenolic profile, determined by UHPLC- ESI/QTOF-MS, showed a greater presence of bound phenols compared to the free ones [2]. Bound phenolic, are covalently bound to cell wall structural components and rod-shaped structural proteins, and in addition to their antioxidant activity, have important effects on the growth inhibition of cancer cells, and in the regulation of the microbiota [3]. The main free phenolic component highlighted was cannaflavin C and the main bound phenolic components were protocatechuic acid, caffeic acid, hydroxycinnamic acid and cannaflavin C. Among the amino acids, hemp flour contains a high presence essential aminoacids (15.9 g/100g). Gliadin and glutenin are completely absent, for this reason, hemp flour is suitable for people with celiac disease. High values of TPC and antiradical

completely absent, for this reason, hemp flour is suitable for people with celiac disease. High values of TPC and antiradical activity have been also highlighted. Although the hemp seeds were previously subjected to oil extraction, hemp flours retain about 8% of oil, and the fatty acids present in the largest amount were linoleic acid (53.6%) followed by -linolenic acid (15.5%) denoting a high nutritional level.

#### Keywords

hemp, flours, waste, byproducts, circular economy, biorefinery

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**INDUSTRY** 

here we have reported the contribution of industry to innovation

# Design Group Italia I.D. Srl

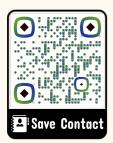
#### Abstract

Design Group Italia is an international design studio. It supports companies in their innovation paths, offering a wide variety of services attributable to six areas of expertise: product design, engineering, branding, space design, service design and digital product design. Its multidisciplinary approach allows DGI to collaborate with companies comprehensively, coordinating all possible touch points between a brand and its customers.

To extend its services to the food industry, DGI has created a food lab, that is a team of designers specialized in product and packaging innovation, who constantly monitor the technological and consumption trends, with special attention to sustainability issues. The Design Group Italia food lab relies on a network of experts (food technologists, nutritionists, chefs, researchers and sociologists), who are involved in the projects when necessary. In the food sector, DGI collaborates with both large companies and PMAs, adapting methodology and budgets accordingly.

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## Food Hub Srl Società Benefit

#### Abstract

Food Hub SRL SB is an innovative startup that facilitates innovation in the agri-food industry to promote progress. The company has three divisions: Media, Academy and Open Innovation, that enable the dissemination of scientific knowledge to industrial stakeholders. Food Hub targets a growing community of over 30,000 stakeholders interested in discovering food innovations. Communication between the scientific research sector and industry is crucial for technological and innovation progress. The scientific research provides a solid base of knowledge and expertise for the development of new technologies and innovative solutions, but to transform these knowledge into practical and sustainable solutions, constant dialogue with industry is necessary. This communication allows for the transfer of knowledge from theory to practice and creates an environment of exchange and collaboration to develop solutions that meet the needs of the market and society. Food Hub plays an important role in this communication by promoting the dissemination of scientific knowledge to industrial stakeholders and facilitating innovation in the food industry.

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### Navhetec S.r.l.

#### Abstract

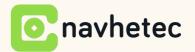
Navhetec S.r.l. is an innovative start-up and Academic SpinOff of the University of Palermo born in June 2016 with the idea to give a new shape to nutraceutical supplements.

The innovation project is perfectly in line with the management team of the innovative startup that has acquired national and international acknowledgement in the field of vesicles (co-founders and R&D sector of navhetec belong to Academia), experiences in business administration (CEO), together with the industrial partnership with Agrumaria Corleone S.p.a, (http://www.agrumariacorleone.com).

Navhetec offers an innovative solution by developing a new way to isolate plant bio-functional compounds with healthy properties. Our products are purified plant vesicles that "naturally" collect and concentrate, in a single structure, several bio-functional elements. Edible plant vesicles are lipoproteic structures, very small bags, with a diameter of about 50 nanometers, identified in several vegetables. Very recent data in literature attributed them curative characteristics depending on the plant species.

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### **PRMFACTORY**

#### Abstract

Thinking Health is the claim of the Thinking and Research in Medicine Factory, PRM Factory. Thinking, therefore actively taking care of Health, is the basis of life and its quality, and for that, it needs a thousand attentions. Doctors nutritionists, pharmacists and wellness specialists are concerned with designing the best possible plan for each person, in which the individual, with his or her lifestyle, plays a fundamental role. Medicine no longer focused only on pathology/drugs but on prevention, cause, person and all-around interventions. Nutrition, lifestyle, environment nutraceuticals rediscover and assume their epigenetic function in a decisive way so that we can truly define complete and innovative medicine with the terms integrated Medicine and Functional Medicine. The formative experiences in different strategic roles, the personal and direct contribution to the development of some important realities in the held, the contacts with the best specialists at home and abroad at Dush PRE to develop a list of very high quality and clinical impact, formulations of extreme interest for four criteria of formulation production.

- Result of research and study of scientific/clinical literature;
- Quality and dosages of raw materials;
- Highest manufacturing standards;
- Innovative technologies to exploit the maximum potential.

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# Developeat

#### **Abstract**

We support startups and companies towards the creation of new food products impacting the future generation. We are here to render food innovation and product development accessible to every company and startup on a mission to save the planet. We stand up in favor of ethical and healthy food development, providing technical insights and support at each stage of the new product development journey. We do not aim simply to make products riding the wave of the latest market trends. Instead, we want to transform the current (outdated) food system and support companies and their game-changing new food projects. With the human population reaching 9.6 billion people by 2050 and global warming rising every year, food products need to be reimagined. At Developeat, we support revolutionary food development projects with a multidisciplinary R&D and NPD assistance tailor-made for truly new food products in the field of plant-based, cell-based and alt-protein space.

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