



UNIVERSITÀ DI PARMA

UNIVERSITA' DEGLI STUDI DI PARMA

DOTTORATO INDUSTRIALE - SOREMARTEC

"SCIENZE DEGLI ALIMENTI"

CICLO XXXII

EXPLOITING THE POTENTIAL OF HAZELNUT BY-PRODUCTS IN A CONFECTIONARY FOOD COMPANY

Coordinatore:

Chiar.ma Prof.ssa Chiara Dall'Asta

Tutor accademico:

Chiar.mo Prof. Furio Brighenti

Tutor aziendale:

Chiar.mo Dott. Roberto Menta

Dottoranda: Mélanie Charron

2016/2019

*“It is not the strongest of the species that survives, nor the most intelligent,
but the one most responsive to change”*

--- Charles Darwin

Contents

ACKNOWLEDGEMENTS.....	VI
ABSTRACT.....	VIII
OBJECTIVES	IX
1. A VISION TOWARD CIRCULAR ECONOMY	1
1.1 CIRCULAR ECONOMY IN A FOOD SYSTEM	2
1.2 EU SITUATION	4
1.3 FERRERO, HAZELNUT VALUE CHAIN AND THE CIRCULAR ECONOMY MODEL.....	6
2. HAZELNUT, THE HEART OF FERRERO	8
2.1 SUSTAINABILITY APPROACH DRIVEN BY HAZELNUT COMPANY	9
2.2 QUALITY IN FERRERO	9
2.3 HAZELNUT NUTRITIONAL PROFILE.....	10
2.4 HAZELNUT MARKET	12
2.4.1 <i>Global</i>	12
2.4.2 <i>Italian</i>	13
2.5 HAZELNUT USED	14
2.6 VALUE OF HAZELNUTS.....	15
2.7 BIO-WASTE FROM HAZELNUT.....	16
2.7.1 <i>Hazelnut Skin</i>	17
2.7.2 <i>Hazelnut Shell</i>	19
3. HAZELNUT NUTRITION RESEARCH.....	20
3.1 HAZELNUT SKIN: AN INTRODUCTION	20
3.1.1 <i>Polyphenolic Composition of Hazelnut Skin</i>	23
3.1.2 <i>Stability of Phenolic Compounds from Hazelnut Skin During Storage</i>	25
3.1.3 <i>Total, Soluble and Insoluble Fibre Content in Hazelnut Skin</i>	27
3.1.4 <i>Phenolic Composition of Different Hazelnut Skin-Based Drinks</i>	29
3.1.5 <i>Cytotoxicity and Genotoxicity of Hazelnut Skin-Based Drink</i>	31
3.1.6 <i>Hazelnut Skin-Enriched Breads</i>	33
3.1.7 <i>In Vivo Toxicology Assay</i>	35
3.1.8 <i>In Vitro Faecal Fermentation of Hazelnut Skin Infusion</i>	37
3.1.9 <i>Colonic Metabolism of (Poly)phenols from Hazelnut Skins</i>	39
3.1.10 <i>γ-Valerolactone, Flavan-3-Ol Metabolites Chemical Synthesis</i>	41
3.1.11 <i>Bioavailability of (Poly)phenols and Acute Effects on Vascular Function by Hazelnut Skin Drink</i>	43
3.2 HAZELNUT SHELL: AN INTRODUCTION.....	45
4. HOW TO VALORISE HAZELNUT BY-PRODUCT IN A CONFECTIONARY COMPANY.....	46
4.1 THE EUROPEAN CONTEXT	46
4.2 THE HAZELNUT BIO-WASTE PROPOSAL	46
4.3 THE STATE OF THE ART	49
4.3.1 <i>Hazelnut Skin Studies in House</i>	49
4.3.2 <i>Hazelnut Shell Studies in House</i>	50

4.3.3	<i>Potentials and Opportunities of (Poly)phenols</i>	50
4.3.4	<i>(Poly)phenols Extraction Process</i>	53
4.3.5	<i>(Poly)phenols from Hazelnut Skin: Opportunity for Ferrero</i>	55
4.3.6	<i>Dietary Supplement</i>	57
4.3.7	<i>Animal Feeding – Ruminants</i>	60
4.3.8	<i>Animal Feeding – Pet Food</i>	61
4.3.9	<i>Cosmetic Sector</i>	62
4.4	NUTWAVE PROJECT: OVERALL CONCEPT	63
4.4.1	<i>Methodology</i>	64
4.4.2	<i>Expected Impacts</i>	64
4.4.2.1	BBI KPI 1: Create at least one new cross-sector interconnection in bio-based economy	65
4.4.2.2	BBI KPI 2: Set the basis for at least one new bio-based value chain	66
4.4.2.3	BBI KPI 3: Create at least two new demonstrated consumer products based on bio-based chemicals and materials that meet market requirements	67
4.4.2.4	BBI KPI 4 Obtain at least 20 % more value from the used new/alternative feedstock than state-of-the-art methods.	68
5.	CONCLUSIONS	69
5.1	RELEVANT SOCIAL, SUSTAINABILITY AND HEALTH IMPACTS	69
5.2	NEW MARKET OPPORTUNITY FOR EU COMPANIES	70
5.3	CONTRIBUTION TO OTHER IMPORTANT IMPACTS (ENVIRONMENT, SOCIAL, SMEs).....	71
5.4	BARRIERS AND GUIDANCE	72
	REFERENCES	74
	WEBSITES	88

Acknowledgements

When the opportunity to do an Industrial PhD with Parma University in collaboration with Soremartec came three years ago, it was far away from my mind to apply: I was forty years old, with two children a busy career and a very busy life. At the time, I felt that it was an opportunity for younger people who have the energy and desire to prove themselves. What a surprise and honor it was when Professor Brighenti and Dr Menta strongly suggested me to accept the challenge: I was the candidate they wanted, the person able to open up a new path for future editions of this Industrial PhD. “It is a project that requires maturity, experience, involvement and passion”. It was enough to convince me to accept the challenge and make from this PhD, an exciting and challenging project.

My sincere thanks goes to Professor Brighenti and Dr Menta for having trusted me, for having supported and encouraged me along this project. Professor Furio Brighenti, my Academic tutor, guided me throughout this thesis and shared with me his brilliant insights despite his overwhelming schedule. I thank him wholeheartedly for giving such thoughtful feedback. I thank Dr. Menta, Director of the Department of Nutrition and Sustainability of Soremartec, also because this thesis is the fruit of a collaboration of several years with him. It was through Dr. Menta that I understood what rigor and precision stand for. This work was possible thanks to his guidance and his involvement. From the outset, his support and daily encouragement fostered a challenging and inspiring work environment. Under his guidance, I successfully overcame many difficulties and learnt a lot. I cannot imagine having a better advisor and mentor for my PhD.

I extend my thanks to Daniele Del Rio and Chiara Dall’Asta, both Professors at Parma University, for the practical tips. Both gave me great help on the operational side of the project and answered calmly and patiently to my frequent questions.

Special thanks go to my teammates from Nutrition and Sustainability Department, especially Ileana Manera and Federica Manini who worked day and night to make the NUtWave project a European-scale project. Without them, I would not have had the access to all the information and clear view of the huge work behind this project. In addition, I would like to

thank Sofia Taini. I really appreciate her constancy to careful review my text and help me to bring everything together.

My thanks also go to my family, specially my husband Giordano: the person who convinced me that running my first half-marathon (moreover on the Great Wall of China) and starting an Industrial PhD was a big opportunity to add something new to my career.

This thesis is the culmination of my PhD journey, which was just like running a trail with a high peak; climbing gradually with encouragement from people I trust to overcome the hardships and frustrations. When I found myself at the top, experiencing the feeling of fulfillment, I realised that, although only my name appears on the cover of this thesis, many great people have contributed to accomplish this huge task.

--Mélanie Charron

Abstract

In order to apply practically Circular Economy Model, Ferrero, worldwide Confectionery Food Company, evaluates the possibility to demonstrate cost-effective and sustainable exploitation of the hazelnut biomass that allows increasing value through the extraction from waste streams and valorisation of bioactive ingredients to be used in consumer products for dietary supplements, food, animal feeding, cosmetics and packaging.

Ferrero hazelnut project undertakes a holistic and circular approach of hazelnut value chain, from “farm-to-farm” including crop production, hazelnut processing, extraction of bioactive compounds ((poly)phenols and fibre); valorisation of the bioactive compounds and closing the loop with farm sector that may use biochar application as fertiliser. Ferrero ambition is to bring together different sectors stakeholders to demonstrate, assess and optimise the sustainability performance of compounds from the new hazelnut value chain. This project generates multiple cross-sector new interconnections through the participation of partners that are not traditionally directly involved.

Ferrero is evaluating the opportunity to develop a range of products using the bioactive compounds. Compounds and products will be evaluated and documented to meet all regulatory requirements and to correspond to regulatory and market standards. Dietary supplements, fibre enriched food products, animal feed or additive with bioactive properties (example: antioxidant, potentially active antimicrobial...) improving animal health and performances, pet food rich in (poly)phenols, skin care cosmetic products with (poly)phenols and make-up cosmetic products with fibre and biochar for industrial and agricultural uses are some potential development products evaluated.

This thesis will focus mainly on the hazelnut skin stream and its health benefits. Such knowledge could be used to improve health in general, reducing the negative impact of the bio-waste through a circular economy approach and thereby contributing to sustainable development for the Company and for future generations.

Objectives

The overall aim of this thesis was to provide new information based on the European situation as regard the circular economy, an innovative business model for a Food Company, in compliance with modern industrial practice of a Confectionary Company.

Specific objectives were to describe how bio-waste of the hazelnut could add value to the hazelnut supply chain. Biomass-based value chains are discussed referring on data from the project, to demonstrate their potential impact and how (poly)phenols from skin can be valorised and be applied in new sector markets.

1. A Vision Toward Circular Economy

Current production economy is based on the linear model “take-make-use-dispose” (Jurgilevich et al., 2016, Lovins et al., 2014, Ward et al., 2016) which assumes that economic growth can be based on the abundance of resources and unlimited waste disposal (Graedel et al., 1994). This model relies on large quantities of cheap, easily accessible materials or energy, and is reaching its physical limits (Bocken et al., 2016).

The concept of a Circular Economy was introduced among others by Pearce in 1990 (Pearce et al., 1990) and has been conceptually developed more and more globally over last decades, in particular by China (Geng et al., 2012), South Korea and the United States (Ghisellini et al., 2016), who were the firsts to start research programs to foster circular economies boosting remanufacturing and reuse (Stahel et al., 2016, Murray et al., 2017). More recently, its application has also been seen in western economies such as in Europe that is taking baby steps towards a Circular Economy approach, helped and boosted by initiatives of NGO like Ellen MacArthur Foundation (MacArthur, 2015).

Defined by Ellen Macarthur Foundation as “the economy model that is restorative and regenerative by design, and which aims to keep products, components and materials at their highest utility and value at all times, distinguishing between technical and biological cycles”, circular economy is seen as the new business model which offers tools to enhance and optimize for sustainability within the Western food system (MacArthur, 2013, MacArthur 2015).

This concept has spread globally over last decades, but the transition has still to overcome different obstacles and limits, such as lack or unclear legislations, insufficient incentives, difficulty in robust LCA models development (Eriksson, 2015) and resiliency of consumers and companies’ mind-set. Despite these problems, Circular Economy potentiality appears to be enormous across different sectors, among which buildings, mobility, mobile phones, clothing and food. While climate change issues increase and resource exploitation is excessive, the circular economy could be one of the answer to the system.

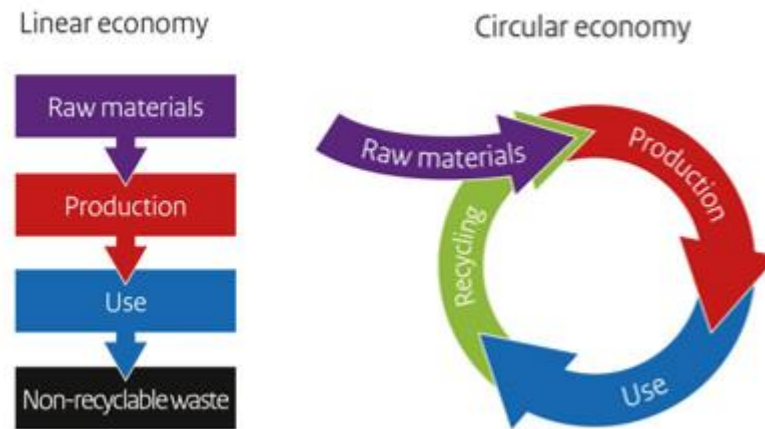
1.1 Circular Economy in a Food System

Applying the Circular Economy concept in a complex and wasteful sector like the food system could seem to be very challenging for the characteristics of raw materials themselves, perishable and easy to be polluted, considering also the pivotal requirement of health security. However, the current inefficiency of the food industry permits to imagine and study infinite applications of Circular Economy through the whole supply chain, with enormous positive perspectives in terms of availability and quality of goods for consumers with a parallel reduction of virgin resources consumed.

Rapid global population growth and increases in demands for food and changes in dietary habits create challenges to provide universal access to healthy food without creating negative environmental, economic, and social impacts. Therefore, our current food production and consumption habits are unsustainable (Foley et al., 2011). Food production generates various environmental impacts, such as eutrophication and increased CO₂ emissions. As per different estimates, approximately 30%–50% (Gustavsson et al., 2011, Jurgilevich et al., 2016, Stuart et al., 2009) of food intended for human consumption is wasted at different stages of the food system (Eriksson, 2015, Papargyropoulou et al., 2014). Although this approach has been successful accompanying economic growth of last decades, the perspective of future population growth with consequent increased exploitation of planet's natural resources, already strained past their possibilities, requires a shift towards a more sustainable and efficient production attitude.

The demand of biological raw materials is rising with the growing population and greater prosperity in the world, with the consequent risk of becoming increasingly scarce. Feeding 10 billions of people by 2050 (Matson et al., 1997) and increasing wealth encouraging more consumption of rich protein food, the system will need to produce 70 percent more food calories in 2050 than at the beginning of the century (Fisher et al., 2009) and enhance nutritional quality. Numerous studies have shown that the food supply chain is already jeopardising world health and consequently human well-being: it is a major cause of greenhouse gas emissions, unsustainable water extraction and pollution, deforestation and biodiversity loss (WHO, 2005). Therefore, the available natural resources must be used as efficiently than today.

Circular Economy can be one of the solution: it aims to keep materials, components and products at their highest utility and value, increasing their circulation and decreasing negative externalities in order to preserve and enhance natural capital. In a circular economy, the central goal is to retain and create as much value as possible from resources whereas, a linear model deals with raw materials in an inefficient way, because the emphasis is not on their conservation.



*Fig. 1 From a linear to a circular economy: Description of a production process in different economies.
FONTE: official site of Government of the Netherlands*

The Circular Economy approach is applicable in all stages of the food system and it has enormous possibilities to improve sustainability and efficiency of the supply chain, minimising upstream inputs and circulating downstream residues/by-products, where possible via technological pathways to maximise utilisation of natural resources.

The Circular Economy approach is a sustainability concept concerning all sectors of industrial production. Circular Economy in the food system implies reducing the amount of waste generated, re-use of food, use of by-products and food waste, nutrient recycling, and changes in diet toward more diverse and more efficient food patterns. In the end, the aim of circular economy is not only to decouple environmental pressure from economic development but also to create and capture new value for businesses, and add extra dimensions to supply chains.

1.2 EU Situation

Recently it is more and more expected in the EU to consider the Circular Economy concept also in the development of food industry. EU has taken a leading global role in value creation in the food industry, the innovation drive for the products, their processing and distribution and consumption phases, being one of the strongest assets. At EU level, the circular economy offers an opportunity to reinvent our economy, making it more sustainable, to enhance global competitiveness, and to generate new jobs (PBL, 2017). In December 2015, the European Commission adopted the EU Action plan for the Circular Economy to support the transition to a more sustainable economic model. The Circular Economy has strong synergies with the EU's objectives on climate and resources and the EU's commitments to implement the 2030 Agenda for Sustainable Development and the SDGs within the EU. (Geng et al., 2013)

In a Circular Economy, the value of products and materials is preserved as long as possible in the value chain. Waste and resources use are minimised, and when a product reaches the end-of-life stage, it is recycled or transformed to be used again to create further value. A Circular Economy model will preserve resources, some of which are increasingly scarce, subject to mounting environmental pressure or volatile prices, and will save costs and create added value for European industries. Food system in particular is inefficient and wasteful through the whole supply chain, from environmental impacts of agriculture and livestock production, to food losses and waste occurring at processing, manufacturing, retail and consumption stages, producing at the same time unhealthy nutritional outcomes.

In this context, Circular Economy has great possibilities to improve sustainability and efficiency of the food supply chain: in agriculture, correct water exploitation (Gleick, 2003) and nutrients flow can be increased through machine innovation and precision farming, while residue streams can be valorised converting them in high-value products and closing in this way internal or external cycles.

Raising livestock for meat consumption has clear impacts on the environment while plant-based foods tend to have a smaller impact. Reducing production and consumption of food derived from animals can lead to health and environmental benefits (Garnett, 2013). Residues production should be prevented or reused effectively with high-value return also in food processing. Food losses and

avoidable food waste can be prevented, while unavoidable wastage can be seen as useful resource inside the food system itself, in animal feeding or in other bio-based industries. Transition would be possible reconsidering food and waste regulations and analysing experiments at niche level in order to recognise opportunities and limits for potential upscale to mainstream practices. This perspective requires changes in infrastructures and technologies, as well as in consumer's responsibilities, practices, and in global production patterns.

Analysing in depth food industries, several steps could be done to improve value preservation of raw materials, water and energy, increasing feeding population opportunities as well as reducing negative environmental and economic consequences. For example, it can prevent food losses by optimising manufacturing processes and redistribution of edible but non-sellable food; it can extract new value from by-products generated during production processes by using them as animal feed or as useful inputs for other industries, or while unsuitable, as biomass for fertilisers and energy; it can contribute to improve packaging design to enhance shelf life and overall environmental footprint of products; it can lead to better recovery and reuse of water, heat and steam from processes, internally or creating connections with other industries.

The food and drinks industry is one of the most important industry sectors throughout the European Union. In the European Union, each year, food industries produce nearly 300 million of tons of organic by-products. The high volumes of solid wastes generated in the agro food industry are not only a potential environmental problem but also an economic burden for companies in terms of their management and represent an additional cost for their disposal.

In the agro food chain, where waste prevention options are either limited or not possible, a different approach toward valorisation of waste fractions is needed. In this context, the "Circular Economy" can reduce wastes while also making best use of by-products by using economically viable processes and procedures to increase their value. To reach this goal, it becomes necessary on one hand an optimization of the process/product finalized to reduce residues and on the other hand a valorisation of the residue obtained.

With these strategic directions, Europe is aiming to lead the transition towards a post-petroleum society while decoupling economic growth from resource depletion and environmental impact.

Ferrero recognises that transition towards a Circular Economy brings great opportunities for innovation, growth and job creation, ultimately creating value not just for the Company but also for Europe and its citizens at large.

1.3 Ferrero, Hazelnut Value Chain and the Circular Economy Model

Within this vision, Ferrero has evaluated to implement a Circular Economy approach and is striving to integrate the sustainability principles in the business models of its partners along the hazelnut value chain. A specific project on hazelnut is an opportunity for a confectionary company to reach a replicable, circular, economically viable and environmentally sustainable model of integrated value chain for the efficient production of bio-based functional ingredients for high-end markets, starting from the residues of the primary processing of hazelnut crops.

The new integrated value chain model will be implemented following a cascading approach, where all fractions from the process will be valorised to obtain marketable end products, which are fully competitive in terms of cost, quality and sustainability with the respective fossil-based counterparts or other benchmark biomass-based products.

Moreover, the new value chain will be set-up following a circular economy approach, closing the cycle of raw materials and minimising the use of primary resources through the establishment of virtuous models of cooperation among all the involved stakeholders: farmers, logistics providers, bio-based processes developers, product developers in the respective sectors of application (namely functional food, nutraceuticals, cosmetics, pet food, feed, agricultural applications, and more) and, last but not least, consumers.

Hazelnut as the **signature** of exclusive properties

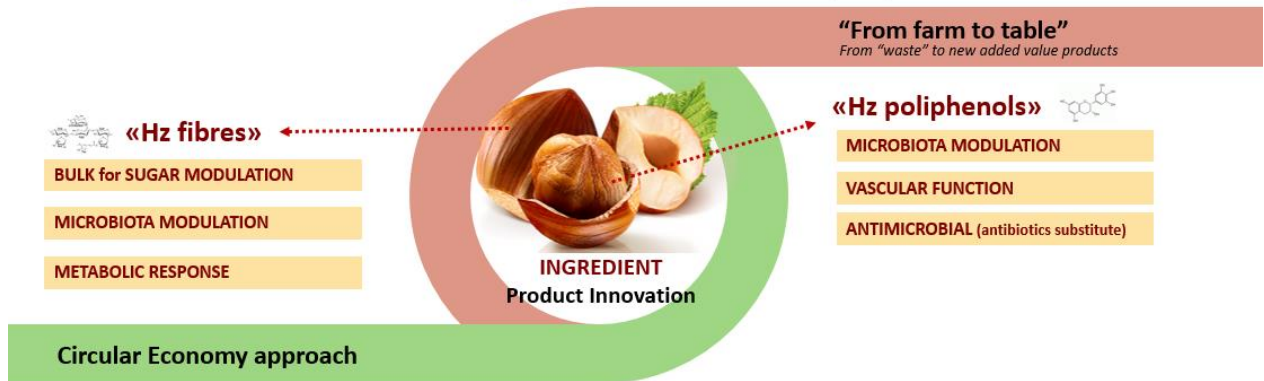


Fig. 2 Circular Economy model apply to hazelnut bio waste.
FONTE : Ferrero Internal Data, 2019

The utilisation of side-streams to create new ingredients is another area for future innovation to be developed under Circular Economy model. The Hazelnut Project vision perfectly fits into the above-mentioned EU policy directions and approach, being able to produce:

- A responsible environmental approach;
- A strong focus on added value along the supply chain, being able to produce substantial economic advantages, mainly in Continental Europe;
- Creation and acceleration of the market-uptake of bio-based products and applications, finding new potential development and/or looking for innovative application in new industrial segment;
- Foster and further contribute to the “Bioeconomy” concept for the Confectionary Food Industry.

2. Hazelnut, the Heart of Ferrero

With a turnover of 10.7 billion Euro, the Ferrero Group is leading the Confectionary market. Ferrero International S.A. consolidated 94 companies worldwide, with 25 operating manufacturing plants. The Group's products are present in more than 170 countries all around the world. The products that led the growth of finished products are the iconic brands like Nutella, Ferrero Rocher, Kinder Joy, Kinder Bueno and Kinder Chocolate.

In 1942, Ferrero began his story in Alba, in the heart of the Langhe countryside, when Pietro Ferrero decided to open a laboratory to experiment and create sweet products. It was a difficult period and, because of the war, even the simplest ingredients had become impossible to find; nevertheless, Pietro did not miss courage and had the brilliant idea of exploiting the treasures available on the spot, i.e. hazelnuts. In 1946 the first Ferrero product was born, a preparation based on hazelnuts named the *Giandujot* (precursor of Nutella), a gianduia paste wrapped in aluminium foil designed to be consumed together with bread. It was immediately a great success. The hazelnut became quickly the protagonist: a hazelnut shelling machine, a roaster, a powder machine and four kneading machines were installed in Pietro Ferrero's laboratory. The current worldwide success of Ferrero Group's products, such as Nutella, Rocher and Kinder Bueno, shows how the intuition to exploit, in the immediate post-war period, a raw material easily available locally (and used to replace part of the cocoa) was indeed a winning bet. In the 90s, Ferrero began to take an interest in the other phases of the hazelnut supply chain. First, the Company explored the agricultural primary production, purchasing land to be dedicated to grow hazelnut in new and potentially productive areas. The first experiment was in Chile with the foundation in 1991 of Ferrero AgriChile. Over the years, the agrifarms of Georgia, Australia, South Africa, Serbia and Argentina were set-up. In recent years, Ferrero has begun to invest also in expanding its hazelnuts processing capacity. The first step was in 2012 with the acquisition of Stelliferi, a leading Italian company in this field. A second important step was the acquisition, in 2014, of the Turkish family group Oltan, world leader in the supply, processing and marketing of hazelnuts. This allowed acquiring new expertise in the selection and processing of the hazelnut. In response to the expansion of activities connected to the hazelnut value chain, Ferrero Hazelnut Company (HCo) division was created in the early 2015.

2.1 Sustainability Approach Driven by Hazelnut Company

Hazelnuts are the heart of Ferrero and have always been a key ingredient in Ferrero leading products. Over the years, Ferrero has worked along the value chain to foster the development of high quality, sustainably grown hazelnuts. HCo division takes care of all hazelnut activities, ranging from cultivation in several geographies and procurement in different markets to the processing of products (Ferrero CSR Report 2017). HCo operates throughout the entire hazelnut supply chain, involving even more employees, people and faces. More than 3000 people work for Ferrero HCo in eight processing plants (5 in Turkey, 2 in Italy and 1 in Chile). Ferrero has six farms around the world: Chile, Argentina, Georgia, South Africa, Australia and Serbia where around 160.000 tons of hazelnuts are produced annually. Ferrero Hazelnut Company is the first “integrated production supply chain company”, which manages hazelnut processing, from the producers to your table (Ferrero Hazelnut Company 2018).

2.2 Quality in Ferrero

Ferrero is the largest purchaser of hazelnuts in the world. To meet the Ferrero quality and quantity requirements, Ferrero purchases only raw, whole and shelled hazelnuts from the last available harvest worldwide. The hazelnuts used in the final products are processed directly in Ferrero-owned plants.

Furthermore, Ferrero has more stringent specifications relating to food safety than those required by current EU legislation. An example are aflatoxins: although the European Union has raised the aflatoxin acceptance limit a few years ago, Ferrero has maintained in its purchasing specifications the earlier parameters, which are four times more stringent.

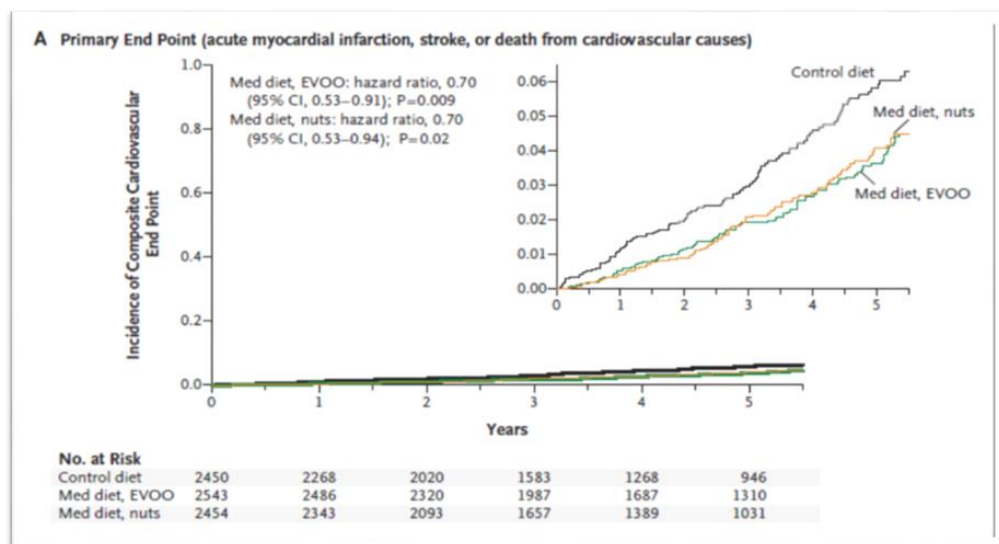
Ferrero also requires its suppliers to carry out specific analyses, according to methods approved by the Group's Quality Management laboratories. On each lot of raw material, these analyses are carried on in addition to those required by local authorities before shipment to the Ferrero production plants.

In addition, a “mild” approach to Hazelnuts roasting is carefully followed. Ferrero tends to adopt lower temperatures and shorter times. Of course, this Total Quality policy leads to an increase in investments in machinery, but allows consumer to have the best roast fit for each recipe.

2.3 Hazelnut Nutritional Profile

In 1990, the World Health Organization (WHO) recommended a minimum of 30 g per day of a combination of nuts, seeds and pulses to be included within a minimum intake of 400 g per day of fruits and vegetables. According to the Food and Drug Administration (FDA), consuming 42g of dried fruit per day as part of a balanced diet and a healthy lifestyle can help reduce the risk of cardiovascular disease.

Recent scientific evidence shows that the consumption of tree nuts, in the context of a balanced diet and lifestyle, is associated with a reduction in body weight over time. Other studies suggest that, due to their satiating effect, a regular daily consumption of nuts can help regulate appetite and the desire to eat. (Tan et al. 2014) The effect of regular incorporation of nuts into the diet is highlighted by the results of the PREDIMED study, where adherence to a Mediterranean diet supplemented with 30g of dried nuts proved to be effective in reducing visceral adiposity and in reducing cardiovascular risk, compared to a “standard” diet.



*Fig. 3 Mediterranean diet in reducing cardiovascular risk
 FONTE: Estruch R. et al. 2013*

The success of dried shell fruit in general and hazelnut in particular, may depend on history and traditions. In the European areas the main nuts crop is hazelnut, a food that contains different nutrients (macro and micro) and bioactive molecules. Belonging to the class of nuts, hazelnut presents all the characteristics of other nut products consumed and appreciated worldwide, such as almond or walnuts.

Table 1 Hazelnut nutritional profile: SFA = Saturated Fat; MUFA = Mono-unsaturated fat; PUFA = Poly-unsaturated fat; LA Linoleic Acid; ALA: Linolenic Acid

FONTE: USDA National Nutrient Database for Standard Reference, April 2018

Dried fruit	Kcal (100 g)	Protein g/100	Carbohydrates g/100	Fat g/100	SFA g/100	MUFA g/100	PUFA g/100	LA g% g/100	ALA g% g/100	(Poly)phenol mg/100g
Hazelnut	642	15	10.4	60.8	4.5	45.7	7.9	7.8	0.09	687
Walnut	668	15.2	6.4	65.2	6.1	8.9	47.2	38.1	9.08	1558
Cashews	564	18.2	5.9	46.4	9.2	27.3	7.8	7.7	0.15	233
Brazilian Nut	669	14.3	8.5	66.4	15.1	24.5	20.5	20.5	0.05	244
Pistachio	569	20.6	9.0	44.4	5.4	23.3	13.5	13.2	0.25	1420
Almond	590	21.3	8.8	50.6	3.9	32.2	12.2	12.2	0.00	287

From a macronutrient point of view, hazelnut can be defined as a fruit with a high nutritional profile. Even more relevant is the quantity and type of micronutrients present in the hazelnut.

The protein content of hazelnut (15% from the USDA food composition database) when tested on European hazelnuts appears higher; on average over 17% with peaks up to 21%. The use of hazelnut as a protein source might therefore be considered, especially in the future when the need for protein food will grow and the search for alternative vegetal protein sources will also be linked to elements connected with the low sustainability of animal protein sources.

Hazelnut proteins are of good biological value and their inclusion in bread-making processes, historically evident in many dietary traditions, allows the supply of foods rich in proteins of high quality.

The available carbohydrate content (energy source) is low, between 6 and 5%, whereas dietary fibre is present in quantities above 10%.

Fats represent more than 60% of total nutrients. They are the main components in hazelnut and the main determinants of its taste, especially after roasting. The acidic profile of hazelnut fat consists of 80% mono-unsaturated and 11% poly-unsaturated fatty acids. The remaining 9% are saturated fatty acids. The Unsaturated / Saturated ratio is on average higher than 13. (Köksala A. I., et al, 2006)

Finally, a further positive characteristic of the hazelnut is linked to its content in (poly)phenols: about 675 mg/100 g. (Del Rio et al., 2011)

In conclusion, the hazelnut is the dried shell fruit characteristic of our latitudes. Hazelnut provides calories but is able, thanks to its structure and composition, to induce phenomena of compensation of the energy intake and provides macronutrients of high biological value and micronutrients of essential value for health. To preserve their nutritional value, it is paramount that hazelnuts are selected with care relatively to crop quality, and processed with an approach aimed at preserving as much as possible their characteristics of natural source of positive micronutrients.

In the food industry, hazelnuts are mainly used as raw materials for their contribution to flavour and texture in the bakery, confectionery, cereal, salad, sauce, dessert and dairy formulations.

2.4 Hazelnut Market

2.4.1 Global

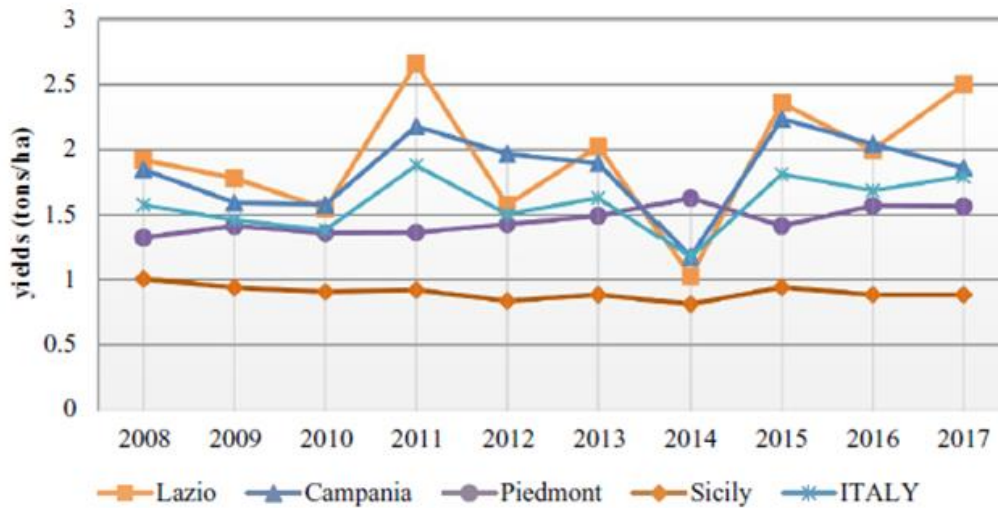
Hazelnut represents 35% of the consumption share of hard-shelled fruits in the world (Kilic et al. 2006). The natural distribution of hazelnut is for the most part in the northern hemisphere, mainly in temperate climates like those found in Turkey, Spain, and Italy. Although Turkey and Italy remain the major producing countries (80% of the world crop), hazelnut cultivation has spread in recent years to new growing areas, including the southern hemisphere (Bottone et al., 2019). World production of hazelnut (with shell) in 2017 was 1.006.178 tonnes (FAOstat 2018). Turkey is the

first producer, with approximately 70 percent of the world's production, followed by Italy (10-15%), the US (4%), Azerbaijan (3%), Georgia, Chile, Spain and Iran. Although hazelnut is one of Turkey's signature crops - with the country accounting for nearly three quarters of the global total - the majority of Turkey's production is exported as a key ingredient in pralines, chocolate spread and numerous other food products manufactured in Europe. Turkey also continues to be the largest exporter of shelled hazelnuts in the world in 2017 with 66% of world exports.

2.4.2 Italian

Hazelnut cultivation in Italy is still growing, sustained by a high international demand both from the chocolate industry and from dietary changes in consumers becoming more and more aware of the benefits of nuts. Italy is the second largest producer in the world, with an annual production of nearly 106.000 tons representing 14,3% of the world production (FAOstat 2018). Its rate of exports is about 11%. Italy is also the first importer in the world with 66.286 tons of shelled hazelnut.

Moreover, Italy plays a central role on the international market of hazelnuts: on the one hand, it is one of the main buyers of Turkish hazelnuts; on the other hand, it also re-exports part of this import as semi-finished products. In particular, 90% of the Italian harvest is directed to the processing industry. The key production areas in Italy are Campania (34% of national production), Lazio (33%), Piedmont (20%), and Sicily (11%). Italian hazelnut production has grown constantly during the period 2008–2017. This increase originated from the Piedmont and Lazio regions, both of which more than compensated the declining production in Sicily. Whilst the four regions (Piedmont, Lazio, Sicily and Campania) under consideration have ideal soil and climate conditions for hazelnut production (growing the local cultivars), crop production at the farm level is affected by variability over time due to climatic factors and pests (Piacentini et al., 2015). The yield data for the period 2008–2017 show a slight increase in Piedmont, Lazio and Campania and a slight reduction in Sicily (Graph.1); this resulted in a slow growth at the national level. Average yield levels differ among the four aforementioned regions: they are higher than the national average (1.59 tons/ha) in Lazio and Campania (1.95 and 1.86 tons/ha respectively), lower in Piedmont and even lower in Sicily (Zinnanti et al., 2019).



Graph. 1 Development of hazelnut yields in the main four Italian regions (tons/ha) – year 2008-2017
 FONTE: Zinnanti et al., 2019

In 2017, the hazelnut sector registered a quantity of 145.000 tons of hazelnut harvested on an area of over 69.000 hectares (ISTAT, 2017). By 2022, Italy is expected to reconvert another 20.000 hectares of agricultural land to hazelnuts crops, equivalent to more than 30% of additional surface area and more than 40% of additional production volume.

Hazelnut production in Piedmont represents 10 % of the total Italian production. In Piedmont, there are three provinces vocated to hazelnut production: Cuneo, in the south-west of Piedmont (80% of the total production), Asti and Alessandria.

The most important cultivars are local: *Tonda di Giffoni* in Latium and *Tonda Gentile delle Langhe*, usually used by Ferrero, have gained the European Protected Geographical Indication (PGI) label.

2.5 Hazelnut Used

Wide applications of hazelnuts have increased the demand for hazelnuts in the market. Hazelnut is a feedstock used in the food industry, especially in the confectionary sector in products such as spreads, chocolate bars, ice cream, dairy products and coffee; they can also be added to a wide array of other products, from cereals and breads to yogurt, soups, salads (Kornsteiner et al., 2013).

Many chocolate manufacturers base their signature products on hazelnut-incorporated product lines, which are emerging as an innovation in taste in the global confectionery market. The key end-users for this market are consumers, foodservice establishments and industries.

Eighty percent of the world hazelnut production is used in the chocolate sector, 15% in cake, biscuit and sweets and 5% are marketed as appetizers (Fiskobirlik, 2003). Ferrero is the world's biggest buyer of hazelnuts, using one third of the world's supply and making ca.180 million kg of its Nutella spread each year (Internal data Ferrero).

There are different alternative uses of hazelnuts; in particular, they are used to make hazelnut oil for cosmetic products, medicinal purpose, personal grooming, massaging and cooking. Moreover, filbert, that is one of the principal flavour compounds of hazelnuts, is used in perfumery (Zarbin et al., 1998).

In recent years, hazelnuts started to be used also in other areas: hazelnut oil is a good source of biodiesel fuel because his chemical content is approximately the same as that of natural oil (Xu and Hanna, 2009).

The increasing usage of hazelnut, especially in confectionary and bakery products, is expected to drive segmental growth. In particular, the demand for hazelnut in the beverages industry segment is projected to increase deeply during the period 2018-2026. In addition, the pharmaceutical industry segment tends to grow, especially in skin ointments. The cosmetics industry segment is expected to register a moderate growth, especially in skin and hair care products (Persistence Market Research, April 2018).

2.6 Value of Hazelnuts

Hazelnut kernel prices can swing as much as 10 percent per week because of unfavourable climate affecting production. Considering the period from October 2018 to January 2019, Turkish in-shell hazelnut sale prices are in a range of 2.12- 2.52 €/kg (according to the conversion from the Turkish lira: 1 EUR = 6,35829 TRY, 1 TRY = 0,157275 EUR last update at 2019-10-29). (GİRESUN COMMODITY EXCHANGE).

The renowned Italian *Tonda Gentile* cultivar has a price range between 9.90 to 11.10 €/kg for industrial destination. (Camera di Commercio Cuneo, October 2019)

Thanks to the high yields of the hazelnut tree, more and more producers are reconverting production from other less remunerative crops.

2.7 Bio-Waste from Hazelnut

The hazelnut is composed by a shell, a skin and a seed, the latter the main component used in the food industry. The fruit processing comprises harvesting, air-drying at 32-40 °C until a moisture content of 4-6%, shell removal and dry roasting at 133-146 °C until a moisture of 1-3% with a belt roaster or roasting drums. After roasting, the seed is cooled and processed by slicing, dicing or grinding. Currently some treatments are performed using method that allow recovering of other parts of the hazelnut.

The skin is obtained by brushing after the roasting process. In fact, during this procedure, the skin becomes dry and crumbly, and can be easily removed from the seed with a gentle abrasion. It is imperative to take off the skin as much as possible because of its richness in tannins - which confer bitter and astringent taste - and because it confers graininess to the pastes since it is milled with some difficulty and not well homogenized. Only few studies attempted to characterize the skin fraction because it has generally been considered a waste, even though it is often present in hazelnut food products because of the difficulty to remove it completely (Cristofori, 2005).

Considering that 50-55% of the entire fruit is represented by the shell and 2% by the skin, the expected increase in production inevitably corresponds to an equal increase in skin availability (Internal data Ferrero, 2017). In line with the EU recommendations, the company is focused on the residues/waste streams from the primary processing of the hazelnut crop. Thanks to the application of circular economy principles, shells and skins from waste can be transformed into new secondary raw materials.



*Fig. 4 Hazelnut and its bio-waste proportions.
FONTE: Internal data Ferrero 2017*

2.7.1 Hazelnut Skin

Hazelnut skin contains about 7.5% moisture, 8% protein, 14.5% fat and 1.7% ash (Anil et al., 2007). Dietary fibre is the main constituent of hazelnut skin, with a percentage contribution of 67.7%, of which 57.7% is insoluble fibre (Özdemir et al., 2014).

AOAC enzymatic-gravimetric methods are utilised in order to measure the content of total, soluble and insoluble fibres. The main steps in these methods include extraction of fats, enzymatic treatments for starch and protein removal, precipitation of soluble dietary fibre components by aqueous ethanol, isolation and weighing of the dietary fibre residue, and correction for protein and ash in the residue (McCleary, 2003).

However, what recently awakened most interest is the (poly)phenolic content of the skin, especially for its potential to be used in different sectors with high value return. The main (poly)phenolic subclasses identified are monomeric and oligomeric flavan-3-ols, which account for more than 95% of total (poly)phenols. Flavonols and dihydrochalcones represent a 3.5%, while phenolic acids are less than the 1% of the total identified phenolics (Del Rio et al., 2011). Catechin, epicatechin, epicatechin gallate, gallic acid, and epigallocatechin gallate represent the majority of flavan-3-ols compounds present in the hazelnut skin (Özdemir et al., 2014), whereas gallic acid is the most abundant phenolic acid (Shahidi et al., 2007).

Flavan-3-ols, also called flavanols, are derivatives of flavans. A monomer catechin, or isomer epicatechin, adds four hydroxyls to flavan-3-ol, making building blocks for concatenated polymers called proanthocyanidins and higher order polymers such as anthocyanidins. Epigallocatechin and gallocatechin contain an additional phenolic hydroxyl group, while catechin gallates are gallic acid esters of the catechin. Regarding benefits of these compounds on human health, the European Food Safety Authority in 2014 approved a health claim for cocoa products containing flavan-3-ols: “*cocoa flavanols help maintain the elasticity of blood vessels, which contributes to normal blood flow*” (EFSA, 2014).

Some studies identified a role of these compounds in preserving the quality of the seed. In fact, (poly)phenols present in the kernel are strictly connected to the stability of hazelnut during storage and to its flavour before and after the roasting process. (Locatelli et al., 2009; Schmitzer et al., 2011)

The complex between phenolic compounds and cell-wall polysaccharides constitutes the so called “antioxidant dietary fibre” that could have relevant physiological and technological implications. Total content of (poly)phenols seems to be different according to the cultivars and their agronomic techniques, such as irrigation.

The extraction of phenolic compounds starts from defatted hazelnut because the lipids can lead to potential modifications and instability of (poly)phenols during the food process. It is better to avoid any possible interference of lipid on hazelnut bioactive compounds and on the evaluation of their functional properties. Hazelnut skin shows a superior antioxidative ability and a higher phenolic content compared to the hazelnut kernel and other by-products. Five phenolic acids have been identified and quantified, one of which is gallic acid and four of which are cinnamic acid derivatives. Gallic acid is the most abundant compound present in the skin, implying the presence of tannins. Tannins are much powerful antioxidants than simple monomeric phenols and may have unique roles in the human digestive metabolism as both savers of other biological antioxidants and protectors of nutrients from oxidative damages (Tokuşoğlu et al., 2011). Moreover their antioxidant properties could give an important contribution to the protection toward atherosclerotic damage. Therefore, hazelnut skins should be considered a source of interesting added value compounds, such as unavailable carbohydrates - particularly soluble fibre - with potential prebiotic properties,

and (poly)phenols – particularly flavan-3-ols - useful to formulate novel functional foods as well as nutraceutical supplements.

2.7.2 Hazelnut Shell

The analysis of hazelnut shell shows that it contains an average of 30.4% hemicelluloses, 26.8% cellulose, 42.9% lignin and 3.3% of other extractive matter (Demirbas et al., 2006). Cellulose and hemi-cellulose are macromolecules made from different sugars, whereas lignin is an aromatic polymer synthesized from phenylpropanoid precursors. Cellulose is a linear polymer that is composed of D-glucose subunits linked by β -(1,4) glycosidic bonds. This polymer forms long chains, elemental fibrils linked together by hydrogen bonds and van der Waals forces. Cellulose is usually present in crystalline form, while a small amount of non-organized cellulose chains forms amorphous cellulose. In the latter conformation, cellulose is more susceptible to enzymatic degradation from the intestinal bacteria (Pérez et al., 2002). In nature, cellulose appears associated with other plant compounds and this association may affect its biodegradation. Hemicelluloses are polysaccharides with a lower molecular weight than cellulose. Hazelnut hemicelluloses are formed from D-xylose, D-mannose, D-galactose, D-glucose, L-arabinose; 4-O-methyl-glucuronic, D-galacturonic and D-glucuronic acids are also present. Sugars are linked together by β -(1,4) and, sometimes, β -(1,3)-glycosidic bonds. The main difference between cellulose and hemicellulose is that hemicellulose has branches with short lateral chains, consisting of different sugars and easily hydrolyzable oligomers. Lignin is linked to both hemicellulose and cellulose, forming a physical seal that is an impenetrable barrier in the plant cell wall. Indeed, its presence in the cell wall provides structural support, impermeability and resistance against oxidative stress and microbial attack. Chemically, lignin is an amorphous hetero-polymer, insoluble in water and optically inactive, formed from phenylpropane units linked together with non-hydrolyzable bonds. This polymer is synthesized by the generation of free radicals, which are released in the peroxidase-mediated dehydrogenation of three phenyl propionic alcohols: coniferyl alcohol (guaiacyl propanol), coumaryl alcohol (p-hydroxyphenyl propanol), and sinapyl alcohol (syringyl propanol). This heterogeneous structure is linked by C–C and aryl-ether linkages, with aryl-glycerol and β -aryl ether being the predominant structures (Sanchez, 2009).

3. Hazelnut Nutrition Research

3.1 Hazelnut Skin: an Introduction

As reported by WHO, cardiovascular disease (CVD) remains the main cause of death worldwide. There are several factors that can reduce or increase the likelihood of developing CVDs and one of the main factors that still require elucidation is the diet. Epidemiological studies have observed a considerable cardio protective effect associated with increased nut consumption. These findings are consistent across a wide range of different nut intakes and across populations differing in gender, age, geographical location and occupation. Based on these findings, tree nut consumption is now considered a qualifying component of a healthy diet.

The benefits of a diet rich in tree nuts have been ascribed to their mono- and polyunsaturated fatty acid content, their high level of dietary fibre and, more recently, to the presence of a number of bioactive molecules in the kernel and skin. These bioactive molecules range from tocopherols to arginine and to (poly)phenols, which might exert positive cardiovascular effects such as LDL protection from oxidation or enhanced endothelial function. In particular, the antioxidant capacity of various nuts and their components has been widely investigated and several studies have acknowledged that nut by-products are especially rich sources of natural phenolic compounds with bioactivity potential. For example, in walnuts, most of the polyphenolic compounds are located in the skin and less than 10% is retained in the kernel when the skin is removed. In most other cases, a significant portion of nut phenolics is located in the skin as well.

Hazelnut skin (poly)phenols are very active in reducing iron (evaluation with the FRAP essay), in fact they have a higher antioxidant capacity compare to other food items (walnuts, coffee, blackberries) and for this reason are very important for health-related effects (Del Rio et al. 2011).

In addition hazelnut skin phenolics compounds are bioavailable: in according to a recent study based on the evaluation on absorption of phenolic compounds from hazelnut skin drink, the estimated bioavailability of (poly)phenols is about 27% (Mocciaro et al., 2019).

Hazelnut (*Corylus avellana L.*), which belongs to the Betulaceae family, is one of the most popular tree nuts consumed worldwide, ranking second in tree nut production after almond. Hazelnut skin, hazelnut hard shell and hazelnut green leafy cover, as well as hazelnut tree leaf, are by-products of roasting, cracking, shelling/hulling, and harvesting processes, respectively and are now investigated for their composition in the attempt to add economic value to waste from the hazelnut industry. As better explained in the following sections, Soremartec, in collaboration with University of Parma and University of Cambridge, has demonstrated that the hazelnut skin is a by-product high in (poly)phenols, mainly monomeric and oligomeric flavan-3-ols, which account for more than 95% of total (poly)phenols. The total antioxidant capacity (TAC) values of the skin ranges from 0.6 to 2.2 moles of reduced iron per kg of sample, which is about three times the TAC of whole walnuts, seven to eight times the TAC of dark chocolate, ten times the TAC of espresso coffee, and twenty-five times the TAC of blackberries.

Moreover, the procyanidin profile of hazelnut skins is partly overlapping with that of cocoa and grape seeds. Endothelial function has been reported to be significantly improved in healthy adults in the initial 2 hours after intake of grape seed phenolics and the acute ingestion of both solid dark chocolate and liquid cocoa acutely improved endothelial function and lowered blood pressure in overweight adults.

Our complete and quantitative profile of (poly)phenols present in hazelnut skins provides the basis to further investigate the potential health effects of hazelnut by-products.

In recent years (poly)phenols have been extensively studied due to their growing commercial value in nutrition, cosmetic and pharmaceutical industry. Different types of plant materials such as crop wastes and residues have also high quantities of these compounds. Every year, thousands of tons of crops wastes are generated in Europe without any substantial use from producers or agrofood-industry sector: this implies an increase in the economic and environmental costs needed for waste management and a loss of potential value. Several recent reports have demonstrated the likely advantages of using crop wastes as a natural source of (poly)phenols, replacing the expensive chemically synthesized antioxidants, anti-inflammatory, and artificial dye composites.

The following part refers to the original studies of nutrition research on hazelnuts carried out internally or externally by Soremartec in collaboration with different Universities and research centres during the last few years. Studies are presented as a short abstract including the main findings that we were able to obtain and that were used as a background for the main project described in this section.

3.1.1 Polyphenolic Composition of Hazelnut Skin

(Del Rio D. et al. 2011)

Introduction

Nuts are a food traditionally associated with the Mediterranean diet and hazelnut (*Corylus avellana* L.) is one of the most popular tree nuts on a worldwide basis, ranking second after almond. Unlike to hazelnut kernels, for hazelnut skins a complete screening of phenolics is still lacking. Therefore, the aim of this work was the qualitative and quantitative characterization of skin (poly)phenols in hazelnut harvested from the main growing areas of the world.

Methods and materials

Nine different hazelnut skin samples, derived by different cultivars and different production areas, have been analysed for their content in polyphenolic compounds by means of HPLC-MS/MS. Moreover, colorimetric assays were carried out analysing the total polyphenol content by means of the Folin-Ciocalteu method and total antioxidant capacity (TAC) with the Ferric Reducing Antioxidant Power assay (FRAP).

Results

The average content of total (poly)phenols of the skin samples analysed, as measured by HPLC-MS/MS, was equal to almost 675mg/100g. The main polyphenolic subclass was by far the monomeric and oligomeric flavan-3-ols, contributing to the total for more than the 95%. Flavonols and dihydrochalcones were responsible of a 3.5%, while phenolic acids were responsible for less than the 1% of the total identified phenolics. The TAC values of the skin samples ranged between 0.6 and 2.2 moles of reduced iron per kg of sample, which is averagely three times the TAC of whole walnuts, 7 to 8 times the TAC of chocolate, 10 times the TAC of an espresso coffee, and 25 times the antioxidant capacity of blackberries.

Conclusions

This investigation produced a complete and quantitative profile of (poly)phenols in hazelnut skins, making this, to our knowledge, the most complete study present in the literature describing the polyphenolic composition of hazelnut skins. This hazelnut by-product, is probably the one of richest edible source of phenolics ever analysed.

3.1.2 Stability of Phenolic Compounds from Hazelnut Skin During Storage

(Carried out by University of Parma)

Introduction

The amount of (poly)phenols presents in food, as well as their total antioxidant capacity, can be influenced by different manufacturing processes and storage conditions.

The aim of this work was to determine the qualitative and quantitative profile of flavan-3-ols, total (poly)phenols content and total antioxidant capacity of hazelnut skins from seven different production area during their storage.

Methods and materials

The hazelnut skins samples were stored respectively for a period of 4 and 8 months at normal refrigeration temperature (5 °C) in two different atmospheres: modified atmosphere rich-in-nitrogen and “environment” atmosphere, i.e. uncontrolled, unmodified room air. Among the seven cultivars analysed, three came from Italy (Tonda Gentile delle Langhe Tonda Gentile Romana, Mortarella) and four from Turkey (Giresun, Trabzon, Ordu, Akçakoca).

Flavan-3-ols were extracted by hot-water extraction then analyzed by HPLC-MS/MS. The TAC (total antioxidant capacity) was assessed by the FRAP method, while total (poly)phenols analysis and quantification (Folin-Ciocalteu reagent) was performed according to the method followed by Singleton & Rossi (1965).

Results

The nitrogen storage proved to be the best one in the first 4 months compared to standard refrigeration storage. In fact, nitrogen storage resulted in both a smaller reduction of flavan-3-ols, the total polyphenol content and a greater increase in antioxidant capacity.

With increasing storage time, the two storage conditions showed almost equivalent effects. In fact, after 8 months of storage there was a significant reduction of flavan-3-ols content that, unlike what

observed at 4 months' storage, was greater in the hazelnut skins kept in a controlled atmosphere at 5 ° C. The higher the polymerization degrees, the lower is the TAC and (poly)phenols reduction. Prolonging the storage time, polymerization processes of the flavan-3-ols may occur.

Conclusions

Among all the different hazelnut cultivars under analysis, those that could be potentially used for the development of functional foods based on skin are Turkey Akçakoca and Ordu ones.

3.1.3 Total, Soluble and Insoluble Fibre Content in Hazelnut Skin

(Carried out by University of Parma)

Introduction

Although fibres cannot be considered a truly nutrient, their consumption with foods has been linked to reduced risk for major chronic and degenerative diseases, such as colon-rectum cancer, diabetes and cardiovascular disease.

The determination of the fibre composition of the hazelnut skin was carried out on samples from different production areas:

- Turkey: AKCAKOCA, GIRESUN, ORDU, TRABZAN
- Georgia
- Italy: GIFFONI, MORTARELLE, TGL, TRG
- Chile

Methods and materials

Hazelnut skin samples, stored during transport in vacuum foil pouches, were finely ground and stored at - 20 ° C until analysed.

For the determination of the fibre, the enzyme kit "Total Dietary Fibre Assay Procedures" (Megazyme, K-TDFR 12/05) was used. For the total, soluble and insoluble fibre characterization, two different methods were applied: AOAC Method 991.43 "Total, Soluble, and insoluble Dietary fibre in Foods "(First Action 1991) and AACC method 32-07 "Determination of Soluble, insoluble, and Total Dietary Fibre in Foods and Food Products "(Final Approval 10-16-91).

Results

See figure below.

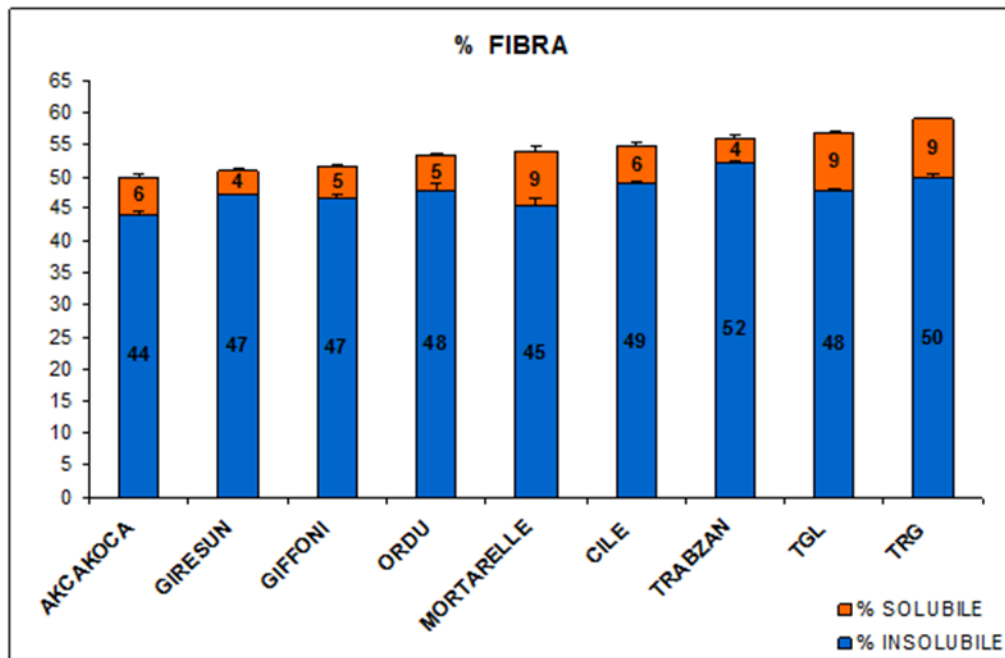


Figure. 2 different percentages of fibre in hazelnut skins.

Conclusions

Total fibre content represents more than 50% of the total weight of hazelnut skins, thus making this side product of the hazelnut supply chain suitable for further evaluation as functional, food-enriching ingredient.

3.1.4 Phenolic Composition of Different Hazelnut Skin-Based Drinks

(Carried out by University of Parma & Cambridge University)

Introduction

The aim of this work was to characterize the phenolic profile in seventeen different hazelnut skin-based drinks, with the intent to select the best one for a bioavailability and bioactivity study.

Methods and materials

Seventeen infusions were prepared considering the following variables:

- 1-3% cuticle concentration;
- Infusion time: 30 to 300 seconds;
- Infusion T: 70 to 95 ° C.

DoE also takes into account the following results:

- Conductivity;
- Colour;
- Polyphenolic profile;
- Organoleptic impressions.

Polyphenolic composition was characterised by UHPLC-MS/MS.

Results

The analyses showed that flavan-3-ols (catechins and proanthocyanidins) are the main subclass of (poly)phenols identified and quantified. There were pronounced quantitative differences among drinks. Notably, three hazelnut drinks had the highest concentration of monomeric flavan-3-ols, particularly catechin, which ranged between 29 and 36 μM . In contrast, other three drinks showed low concentrations (6-9 μM).

In addition to catechins and proanthocyanidins, other flavonoids were identified and quantified: quercitrin was the main one.

Analyses were extended to three drinks having different features: not-filtered, filtered, filtered/centrifuged/filtered. The not-filtered drink showed the greatest catechins and proanthocyanidins concentration (respectively 7 μM and 32 μM). On the other side, the filtered/centrifuged/filtered was characterized by the lowest concentration in both catechins (4 μM) and proanthocyanidins (17 μM).

Conclusions

In the light of these results, the following protocol for drink preparation from hazelnut skin is recommended:

- 1% hazelnut skin
- 7.5% sugar content
- 300 sec infusion time
- 80°C

Among the several drink samples, this protocol provided the best compromise between organoleptic quality and chemical composition needed for testing in human volunteers the putative health benefits of hazelnut (poly)phenols.

3.1.5 Cytotoxicity and Genotoxicity of Hazelnut Skin-Based Drink

(Carried out by University of Parma & Cambridge University)

Introduction

The cytotoxic and genotoxic activity of hazelnut skin infusion and its components, both single and mixed, was evaluated in different human cell lines by MTS assay and Comet assay.

Methods and materials

For cytotoxicity assays, Normal Human Dermal Fibroblasts (NHDF), Normal Colon Epithelial Cells CCD 841 CoN (ATCC® CRL-1790) and Human Colorectal Adenocarcinoma Cell Line HT29 were used. Dilutions in the 0.20%-50% range were tested.

Genotoxicity was tested by Comet assay, using non-cytotoxic concentrations (0.39% and 0.78%) on HT29 cell line. This line seemed to be the most sensible one to hazelnut skin infusion.

Results

Hazelnut skin infusion showed anti-proliferative properties on each of the three cell lines tested. However, HT29 cells showed a higher sensitivity ($IC_{50} = 3.7\%$), compared to the others two normal lines, HF ($IC_{50} = 6.25\%$) e CCD 841 CoN ($IC_{50} = 7.5\%$). In particular, at $0.4\% \div 6.25\%$, concentrations, a clear difference in sensitivity was observed between the two cell lines derived from the gastrointestinal compartment - the colon tumour line HT29 and the normal line CCD 841 CoN.

Genotoxicity: the infusion showed no genotoxic effects at any tested dilution.

The effects exerted by each phenolic component (catechin, epicatechin, procyanidin B2, procyanidin C1, diidrossiphenil- γ -valerolacton (M6) and idrossiphenil- γ -valerolacton (M7)) on HT29 cells proliferation were tested individually. After 24h treatment, 25 μ M catechin and epicatechin reduced cell proliferation, while procyanidins and valerolactones did not show the

same properties. A mix containing catechins and procyanindins showed anti-proliferative activity on HT29 tumour cell line too.

Conclusions

This study does not suggest a potential risk of toxicity at gastro-intestinal level: the potential antiproliferative effect of several components of the infusion against tumour cells is rather interesting.

Ongoing investigations on four additional different cell lines will allow bettering understanding the anti-proliferative effects of these molecules.

3.1.6 Hazelnut Skin-Enriched Breads

(Internal Soremartec research- DTS)

Introduction

Following the results obtained on beverages, the aim of this study was to assess the digestibility and the potential prebiotic capabilities of different types of bread enriched with hazelnut skin after *in vitro* digestion and fermentation.

Methods and materials

Seven breads enriched with hazelnut skin were formulated: four bread had different percentage of hazelnut skin (whole or grinded) and total fibre content; two breads had the same total fibre amount, without hazelnut skin (cellulose used as bulk); one bread was baked using hazelnut skin infusion instead of water. Commercial white bread was used as control.

Breads were analysed for resistant starch content, and *in vitro* digestion and fermentation were performed. In fermented slurries, pH, SCFAs (short-chain fatty acids) and content in (poly)phenols were measured at selected times.

Results

The presence of skin interfered with the development of the gluten network. Therefore, the percentage of small blisters within the fibre-enriched breads was greater. Minced skin interfered more with the matrix compared to whole skin, altering the gluten net and developing smaller alveoli.

In vitro digestion showed that the presence of hazelnut skin was able to modify starch digestibility. Nevertheless, data cannot explain which component of hazelnut skin is responsible for this modification.

In vitro fermentation confirmed the bacterial synthesis of secondary catabolites originated from flavanolic component of hazelnut skin. Moreover, grinded hazelnut skin-enriched bread showed a greater suppression in SCFA production.

Conclusions

The fact that hazelnut skins are likely to interfere with the development of the gluten network during the rising process could reinforce the hypothesis of a potential inhibitory effect of (poly)phenols on yeast growth.

In Vitro digestion demonstrates that 3.5% hazelnut skin-enriched bread performs similarly to white bread for what starch digestion is concerned, while 6% hazelnut skin-enriched bread releases starch at a slower rate.

Hazelnut skin (poly)phenols do not seem to mediate a substantial decrease in the starch release during the digestive process.

The lower SCFA production in minced hazelnut skin-enriched bread may depend on increased availability of phenolic compounds interacting with the intestinal bacterial microbiota.

3.1.7 *In Vivo* Toxicology Assay

(Carried out by University of Parma)

Introduction

The use of hazelnut skins as isolated food ingredient can significantly increase exposure to (poly)phenolic compounds and other components present in the outer layer of hazelnuts. It was therefore considered of interest to evaluate, with a medium-term toxicological assay, the effects of sub-chronic consumption of hazelnut skin in animals (1.000 mg/day/kg body weight).

Methods and materials

A sub-chronic toxicology study was carried out according to the OECD TG 408 guidelines (<http://browse.oecdbookshop.org/oecd/pdfs/free/9740801e.pdf>) for repeated exposure studies, as indicated by EFSA for toxicological evaluation of foods and ingredients (<http://www.efsa.europa.eu/en/press/news/111207.htm>). A single daily dose equal to 1.000 mg hazelnut skin/day/kg body weight was administered for 90 days to adult Sprague-Dawley rats. Rats were then sacrificed with carbon dioxide asphyxiation and biochemical and anatomo-istopathological analyses were performed in order to evaluate the effects of such a massive intake of hazelnut skin.

Results

The treatment, extended for 90 days, did not affect the metabolic balance of the test animals. Even from a neurological point of view, the treatment did not result into deterioration of reflexes, balance, reaction time and hearing, measured according to the OECD protocol.

Repeated hazelnut skin consumption to a level of exposure equal to 1.000 mg/day/kg body weight did not trigger biochemical and anatomo-istopathologic damages; therefore, results suggest no need for further sub-chronic toxicity studies at lower levels of exposure.

Conclusions

This set of experimental evidences, and literature data, allows assuming that hazelnut skin consumption, even at high doses, does not represent a significant risk from a toxicological point of view.

3.1.8 *In Vitro* Faecal Fermentation of Hazelnut Skin Infusion

(Carried out by University of Parma & Cambridge University)

Introduction

The role of the gut microbiota in the production and excretion of phenolic metabolites has been widely described in the last decade. Faecal bacteria living in the colon play a key role in increasing the bioavailability of (poly)phenols originally present in the food matrix. Since these compounds cannot be directly absorbed in the upper gastrointestinal tract, they reach the colon and may then come into contact with the colonic microbiota. In order to evaluate the action of microbial enzymes on phenolic compounds contained in the hazelnut skin, an infusion of hazelnut (cv. Ordu) skin was submitted to *in vitro* faecal fermentation with a faecal starter. A fermentation model, able to reproduce in a simplified way the intestinal environment, was used to this purpose.

Methods and materials

Hazelnut skin (Ordu cultivar) infusions were added to a growth fermentation broth and then inoculated with a suspension of fresh human faeces. The inoculated flasks were incubated for 24 hours at 37°C in anaerobic conditions. Samples were withdrawn at time 0, 5 and 24 hours, and then analysed by UHPLC-MS/MS for phenolic metabolites.

Results

Microbial enzymes produced several modifications of the phenolic compounds initially identified in the hazelnut skin infusion.

After 5 hours, it was no longer possible to observe the original phenolic compounds; however several catabolites derived from flavanols and procyanidins were detected. In particular, two compounds deriving from degradation of flavan-3-ols were identified: 5-(3,4-dihydroxyphenyl)- γ -valerolactone [M6] and 3-(3-hydroxyphenyl) propionic acid [3- HPP].

Conclusions

The study confirms the formation of valerolactones after microbial metabolism of flavan-3-ols. Valerolactones are metabolites that the emerging scientific literature begins to associate with the positive effects ascribed to (poly)phenols-rich foods, such as cocoa, green tea and tree nuts

3.1.9 Colonic Metabolism of (Poly)phenols from Hazelnut Skins (Internal Soremartec research - DTS)

Introduction

The aim of this work was to evaluate the human metabolism of the (poly)phenolic component of hazelnut skin after acute ingestion. The (poly)phenols were administered in two different food matrices: yogurt enriched with minced hazelnut skin and hazelnut skin infusion.

Materials & Methods

In the first test, four subjects ingested 250 ml of yogurt added with 8 g of minced hazelnut skin. Urine was collected before the ingestion (t₀) and every six hours for the next 36 hours. In the second test, three subjects consumed 500 ml 1% hazelnut skin infusion. Urine was collected before the ingestion (t₀) and for the next 24 hours. Samples were analysed by HPLC-MS/MS.

Results

Yogurt: several metabolites derived from epicatechins were identified in the urine in sulphated, glucuronidated and/or methylated form, due to the action of phase II human enzymes at intestinal and hepatic level. These metabolites were not detected in urine before hazelnut skin consumption. Beside conjugated epicatechins, a flavan-3-ols metabolite was also detected: 5-(3',4'-dihydroxyphenyl)- γ -valerolactone. This molecule derives from flavan-3-ols bacterial degradation by the gut microbiota. The valerolactone was detected in its conjugated forms (sulphated, glucuronidated, methylated), indicating an interaction with phase II human enzymes. No variations in the urinary excretory profile were recorded over 36 hours after yogurt ingestion.

Infusion: in addition to epicatechin metabolites, a high excretion of conjugated dihydroxyphenyl- γ -valerolactone were detected. The peak was reached 10 hours after ingestion. The concentration of the sulphated form was 100-fold higher than concentration at t₀.

Conclusions

This experiment confirms that flavan-3-ols, when ingested as intact hazelnut skins, have little/no bioaccessibility and bioavailability, especially in the colonic tract.

Conversely, the high valerolactone excretion after the consumption of Hazelnut skin infusion suggests a good bioaccessibility of native (poly)phenols due to water extraction.

Hot water extraction is so far a compulsory step to ensure a biologically relevant flavan-3-ols bioavailability.

3.1.10 γ -Valerolactone, Flavan-3-Ol Metabolites Chemical Synthesis (Curti C., et al. 2015)

Introduction

Orally administered catechins or procyanidins are not efficiently absorbed at the small intestine level and, consequently, undergo extensive microbial metabolism in the colon, affording ring fission products mainly represented by hydroxyphenyl γ -valerolactone derivatives. The scientific evidence accumulated during the last decade, though, indicates that the beneficial effects of flavan-3-ols in the human organism are mainly attributed not to the parent set of compounds present in the food matrix, but rather to the corresponding enteric metabolites, and in particular to those derived from their microbial catabolism occurring in the colon.

Despite the interesting pharmacological profile exhibited by these phenolic lactones, they are not commercially available: to address this issue, chemical synthesis represents an attractive and viable option.

Methods & Materials

A rapid approach for the synthesis of highly enantioenriched hydroxyphenyl γ -valerolactones, which are biologically effective and scarcely available metabolites of plant-derived flavan-3-ols, was planned.

First, γ -valerolactone skeleton was built, being able to reply its 3-d chiral structure by asymmetric catalysis.

Five phenil- γ -valerolactone targets were obtained in 5–6 synthetic steps. Compounds were produced in their non-conjugated form (sulphated, glucuronidated and/or methylated), that is the compounds produced by gut microbiota after bacterial metabolism.

After that, in order to reply the action of phase II human enzymes, phenil- γ -valerolactones underwent conjugation steps, i.e. glucuronidation and sulphation.

Results & Conclusion

A rapid approach for the synthesis of highly enantioenriched hydroxyphenyl γ -valerolactones, which are biologically effective and scarcely available metabolites of plant-derived flavan-3-ols, was developed.

This synthetic approach could be a good starting-point for further analytical and biological investigations about this major, but little available, bioactive molecule.

3.1.11 Bioavailability of (Poly)phenols and Acute Effects on Vascular Function by Hazelnut Skin Drink

(Mocciaro et al. 2019)

Introduction

Cardiovascular diseases represent one of the main causes of mortality and morbidity worldwide and produce heavy social and economic impact. Many recent studies have suggested that the daily intake of food rich in (poly)phenols, such as hazelnut, is associated with lower risk of all-cause mortality and CVD.

The aim of this work is to investigate the potential health effects of (poly)phenols correlating acute ingestion of hazelnut skin drink with vascular /endothelial function.

Material & Methods

After screening visits, 41 healthy eligible volunteers (adults) were analysed in a single blind, non-randomised crossover trial. They consumed a placebo drink (238 ml of water and 5 grams of sugar) during one occasion and a hazelnut drink (238 ml of hazelnut skin infusion and 5 grams of sugar) during a second occasion in random order primary endpoints were:

- Concentration of urinary hazelnut phenolic metabolites ;
- Concentration of plasmatic hazelnut phenolic metabolites;
- Polyphenolic composition and bioavailability.

Results

Using UHPLC-MS/MS, the polyphenolic profile was characterised and the amount of flavan-3-ols was determined. Hippuric acid and 10 metabolites derived from metabolic transformation of flavan-3-ols were identified in plasma samples with a concentration range between 0,5 nmol/L to 4 nmol/L, while 26 metabolites were detected in urine samples. Acute ingestion of the test drink did not show any statistically significant effect on vascular measurements: there was no correlation

between hippuric acid and vascular effects. Participants were classified as high- and low-metabolite producers and a trend was observed with high-producers of certain secondary metabolites. Bioavailability was estimated at about 27%.

Conclusions

This work demonstrated an effective absorption of phenolic compounds from hazelnut skin drink. Despite the fact that hazelnut skin phenolics were highly bioavailable, the present study did not find any significant acute effects of the hazelnut skin drink on vascular/endothelial function in healthy subjects.

3.2 Hazelnut Shell: an Introduction

EFSA fibre intake recommendations are based upon the amount needed to keep correct bowels function. The acceptable intake is 25g per day. Moreover, there is evidence that consuming fibre-rich foods, such as wholegrain cereals, fruits and vegetables providing more than 25g of fibre per day, aids weight control, possibly through their satiating and slightly laxative properties. Fibre consumption also shows positive effects on blood lipid markers (Ghada, 2019). On the other hand, many studies highlight how low fibre intake is within Western diets. In EU, the average intake of total dietary fibre is generally lower than recommendations, ranging from 12 g in Northern Countries to 29 g per day in some Mediterranean areas.

In recent years, fibre has also been studied for its prebiotic effect. Prebiotics are defined as “*a non-viable food component that confers a health benefit on the host associated with modulation of the microflora*” (FAO 2007). The prebiotic effect is associated with an increase in the bacterial groups that exert beneficial effects on gastro-intestinal health of the host (bifidobacteria, lactobacilli, and eubacteria) together with a possible decrease of less desirable bacterial groups – pathogen or opportunistic ones - such as clostridia, enterobacteria and some E. Coli strains.

Fibres are also very good bulking agents in reformulation approach due to their structural properties, providing low energy density to the final product.

Actually, hazelnut kernels are considered as burning material for domestic and industrial uses in many places. However, this agri-food waste can be used both as fermentation substratum and as a fibre ingredient added to foods, either dietary or prebiotic ones.

During my PhD work, I was involved in the Fibre project where we successfully extracted a prebiotic fibre family, namely arabino-xylo-oligosaccharides (AXOS), from hazelnut shell by a steam explosion process. This fibre was characterized and the prebioticity was assessed with the aim to create added value to the hazelnut supply chain by producing dietary fibres and other high-values compounds from hazelnut shell.

For confidentiality reasons and to avoid any issue with patent and novel food approval procedures Soremartec may want to apply for in the future, I decided not to report the previous studies and researches Soremartec has done in the past years.

4. How to Valorise Hazelnut By-Product in a Confectionary Company

4.1 The European Context

As mentioned in the Chapter 1, the circular economy approach is a clear priority for the European Commission. Action at EU level can drive investments, create a level playing field, and mitigate obstacles originating from European legislation or its inadequate enforcement. The European Commission is funding circular economy projects under several EU programmes, such as Horizon 2020, including the SME Instrument LIFE and others.

The Bio-Based Industries Joint Undertaking (BBI JU) is a €3.7 billion Public-Private Partnership between the EU and the Bio-based Industries Consortium. Operating under Horizon 2020, this EU body is driven by the Vision and Strategic Innovation and Research Agenda (SIRA) developed by the industry. Ferrero is a member of the Core team of BBI since 2017 and in 2018, Ferrero became an active member by applying to a call. The objective that BBI and Ferrero would like to reach is to find a business models that integrate economic actors along the value chain from supply of biomass to users of bio-based materials, including creation of new cross-sector interconnections and support of cross-industry clusters.

4.2 The Hazelnut Bio-Waste Proposal

Considering hazelnut as a starting point, Ferrero set-up a project that aims to be a model of circular economy in a Confectionary Company. The Hazelnut Project idea is based on the valorisation of hazelnuts' side-streams resulting from the processing cycle of the company. The aim is both to improve management of the side-streams and to optimize their cycle by developing new production facilities to valorise their use as added-value products.

Hazelnut skin and hazelnut shell, as well as hazelnut green leafy cover and hazelnut tree leaf, are by-products of roasting, cracking, de-hulling, and harvesting processes, respectively (Shahidi et al., 2007). These by-products do not present any commercial value except for the hazelnut hard

shell, which is used as a heating source upon burning, though with very low value return. However, those by-products, in particular shell and skin, may present interesting features and are currently investigated in the attempt to add economic value to processes residues from the hazelnut industry. The reason of this impulse is simple: as seen in Chapter 2, world production of hazelnut with shell is around 1 million tons. Considering that the shell represents more than 50% of the total weight of the nut, whereas the skin is around 2%, it appears clear that flows of these by-products are highly relevant.

The project idea was born from the willing of Ferrero to exploit hazelnut's shell and skin residues leading to reducing waste and obtaining products of higher value on the market. Nowadays solutions are in various stages of development for products derived from skin and shell. From these raw materials, 2 major classes of high added-value products can be obtained: edible dietary fibre - namely arabino-xylooligosaccharides (Axos) - with selected and top functional characteristics, and substantial amounts of (poly)phenols - mainly flavan-3-ols - that can be used in several ways by different industrial segments (i.e. Food and Feed, Cosmetics and nutraceuticals). With emerging technologies, the possibility of using these agri-food waste streams as alternative source for bioactive ingredients is becoming more and more viable. The valorisation of hazelnut shells and skins depends on successfully addressing challenges inherent to their logistics, the characterisation of the bioactive components, the development of consumer products and the development of high-end markets for such products.

The Hazelnut Project will assess and optimize (at a pre-industrial scale) a steam explosion process to obtain AXOS fibre from the hazelnut shell and a extraction process of (poly)phenols from hazelnut skin to provide bio-active compounds for different value chains and identify suitable end products for further improving and upscaling.

In particular, steam explosion process is a very versatile and clean technology that uses steam or liquid water at high-temperatures as the only solvent. It represents a promising solution to treat several recalcitrant biomasses at a pre-industrial scale, such as a variety of feedstock from forestry, agriculture, industry or urban solid wastes. In fact, much of the lignocellulosic biomasses are not easily processed and highly resistant to chemical and biological degradation due to their molecular architecture. Steam explosion is one of the most energy efficient and environmentally friendly pre-

treatment methods for lignocellulose pre-treatment. The lack of organic solvents and corrosive chemicals makes it attractive for industrial-scale use. (A Shrotri, et al., 2017)

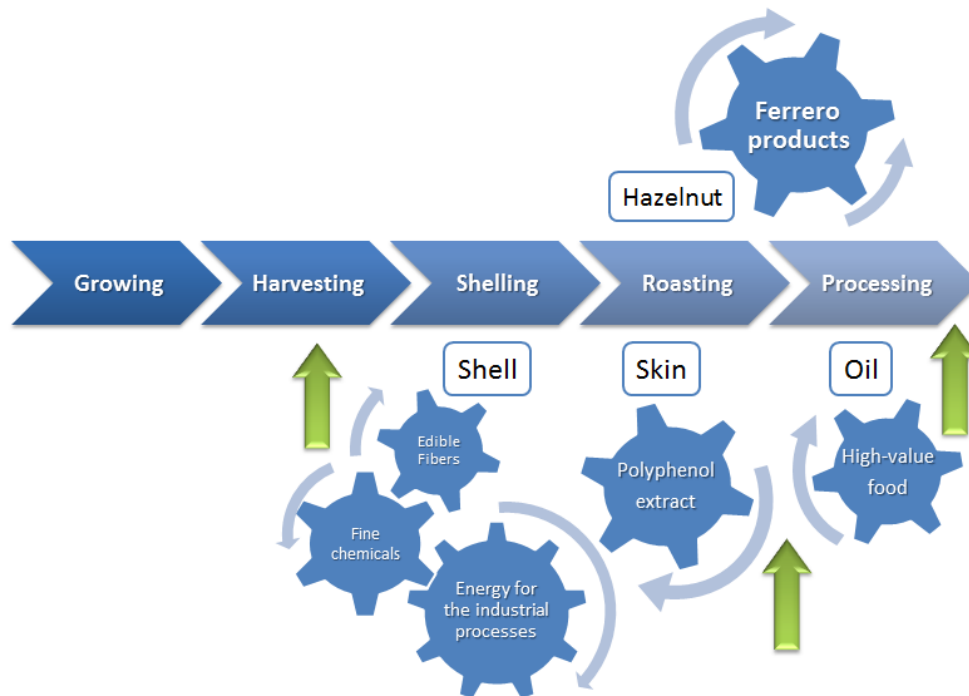


Fig. 5 Added values along hazelnut supply chain
 FONTE: Internal data Ferrero

The Hazelnut Project’s approach could be replicated for application on other huge amounts of lignocellulosic biomasses, allowing the valorisation of by-products obtained not only from hazelnut but also from commodities such as sugar cane bagasse, sweet sorghum, hardwood, softwood, corn cobs, corn stoke, rice straw, nut shells, wheat straw and banana waste.

The project aims to create and accelerate the market-uptake of bio-based products and applications, finding new potential developments and/or looking for innovative applications in new industrial segments. In the next future, growing demand for functional ingredient is expected to drive the market. In particular, this demand is driven by increasing consumer awareness towards nutrition, health and amplified emphasis on the importance for healthy ingredients in diet.

With this project focused on using bio-waste from hazelnut, Ferrero will demonstrate cost-effective and sustainable exploitation of the hazelnut biomass through a circular economy approach. This will allow increasing the value of the biomass through the extraction from waste streams and valorisation of bioactive ingredients through their use in products for dietary supplements, food, animal feeding, cosmetics and packaging.

In addition, the project will establish cooperation and partnership with industries, research centres and other partners that will help exploiting the value chains for these specific applications with a clear return in improving the environmental profile of the company and its scientific credibility. Building blocks that together form platforms make an efficient circular economy model.

The expected outcome will include higher awareness and acceptance of the company brands by consumers and market sectors, hence improving Ferrero competitiveness and contribute to the EU bio-based industry.

4.3 The State of the Art

The studies performed by Soremartec in collaboration with different Universities and research centres during the last few years on fibres and (poly)phenols from hazelnut shells and skins (compare chapter 3), and some other independent scientific papers provide a solid preliminary set of data to demonstrate the achievability of the project objectives.

4.3.1 Hazelnut Skin Studies in House

- Polyphenolic Composition of Hazelnut Skin (Del Rio et al., 2011)
- Colonic Metabolism of (poly)phenols from Coffee, Green Tea, and Hazelnut Skins (Calani et al. 2012)
- An exploratory study profiling secondary polyphenol metabolites and acute modulation of vascular function following ingestion of a hazelnut extract based drink (University of Parma – Medical Research Council MRC Cambridge - 2015-2017)
- Stability of hazelnut skin phenolic compounds during storage (University of Parma - 2016)

- Cytotoxicity and genotoxicity of hazelnut skin-based drink (University of Parma - 2016)
- *In vitro* study on hazelnut skin (poly)phenols effects on “AGE” (advanced glycation end-products) associated cellular damage (Campus Biomedico di Roma, 2019).

4.3.2 Hazelnut Shell Studies in House

Soremartec has been able to successfully extract through a steam explosion process a prebiotic fibre - (A) XOS from hazelnut shells, which has been characterized for its pre-biotic properties.

- Steam explosion preliminary lab test extraction (ENEA, 2013)
- Determination of in-vitro prebiotic properties of shell hazelnut extract (AAT, 2013-2014)
- Search of the toxicological information available for a number of potential compounds in hazelnut shell extract (Melete srl, 2016)
- Steam explosion extraction trials performed in batch pilot plant (30 L reactor) (BPF, 2017)
- Chemical characterization by multidimensional NMR and HPAEC/PAD of the Hazelnuts AXOS extracted (Wageningen University WUR – Soremartec Chemlab)
- Life Cycle Assessment performed by Exergy approach of the steam explosion process (WUR, 2017)
- Steam explosion and hydrothermal treatment extraction trials performed in batch pilot plant (30 L reactor) (VTT, 2019)
- Comparison in terms Chemical composition and prebiotic efficacy between fibre form hazelnut shells and other similar fibre on the market (VTT, UCSC 2019)

4.3.3 Potentials and Opportunities of (Poly)phenols

It is extremely difficult to estimate the average daily intake of (poly)phenols due to structural diversity, lack of standardized analytical methods and variation of content in a particular foodstuff. However, most authors referred an approximate daily intake of about 1 g/day. (Scalbert 2000). Nowadays the currently existing data are insufficient for the development of applicable dietary guidance on the intake of flavanols and procyanidins or to determinate a minimum intake amounts necessary to achieve population-based health benefits. (Ottaviani 2018)

(Poly)phenol intake is also affected by intrinsic factors such as the geographical area, the population characteristics in term of age, gender and socio-cultural factors and above all the dietary habits and preferences. (Del Bo' et al., 2019)

In addition, large variability in terms of methods for the evaluation and quantification of (poly)phenol intake, markers and endpoints considered, makes it still difficult to establish an evidence-based reference intake for the whole class and subclass of compounds.

If there is a lack of a recommended amount of (poly)phenols, in Italy for example, “Ministero della Salute” indicated a maximum daily intake about some classes, such as flavonoids (1000 mg/day) or isoflavones (80 mg/day). (Ministero della salute, 2009)

Many articles have estimated that in European countries the mean intake is about 900 mg/day, while in North and South America is about 800 mg/day. (Ottaviani 2018) Within the EPIC study, Denmark showed the highest intake of total polyphenols (1786 mg/day) while Greece the lowest (584 mg/day). (EPIC STUDY 2015)

In sight of these numbers, in many countries, there is a gap between the effective intake and the recommended one.

The use of botanicals and dietary supplements derived from natural substances as an adjunct to an improved quality of life or for their claimed medical benefits has become increasingly common in western countries (Abdel-Rahman et al., 2011, Ahn, 2017). The size of the global market of botanicals and dietary supplements, including functional foods for nutrition and health and medical supplies, is estimated to be 1 trillion dollars and is growing annually by 8 to 10 %. About half of the medical supplements currently on sale are of botanical origin or are extracts composed of single-element substances obtained from natural products (Ahn, 2017). Among the different phytochemicals used by the food and beverage , health, cosmetic and animal nutrition industries, (poly)phenols or phenolic compounds are those attracting more attention due to their antioxidant and health-promoting properties (Del Rio et al., 2013, Rodriguez-Mateos et al., 2014). Phenolic compounds are one of the most abundant and ubiquitous groups of plant secondary metabolites, occurring in a wide number of foods and beverages (Pérez-Jiménez et al., 2010). (Poly)phenolic compounds are produced in plants by a plastic system of biosynthetic pathways and are involved in a plethora of physiological and ecological roles (Crozier et al., 2009). Their roles and ecological

significance span on a wide array of biological activities, chemical diversity and abundance. Despite being mostly considered in the past as antinutritional food constituents (and this can still be an issue for animal nutrition), their role as healthy compounds when introduced in the human diet at proper amounts is now clearly emerging.

Moreover, growing health awareness among consumers, coupled with the growing inclination for safe, naturally-sourced products, has been a driver for the global market of (poly)phenols. The (poly)phenols market value was valued at \$757 million in 2015, and is expected to reach \$1,121 million by 2022 and \$1,330 by 2024, supported by a CAGR (Compound Annual Growth Rate) of 8.26% during the forecast period 2016 - 2024 (Allied Market Research, 2017; Grand View Research, 2016). Based on current trends, there is anticipation of further boosts in the market from 2016 to 2024 due to increasing usage of polyphenol extract in the food, beverages, pharmaceutical, and cosmetic industry (Allied Market Research, 2017). In this sense, the market holds a substantial opportunity of growth globally during the next 5 years. In terms of utilization, the global (poly)phenols economy is led by the functional beverages sector (44%), followed by functional foods (33%), primarily as a result of the strong demand for polyphenol-rich drinks in the form of juices, energy drinks, and enhanced water in most developed countries (Grand View Research, 2016). Thus, growing demand for functional beverages in the healthcare, sport, and entertainment sector is one of the key factors driving the development of the (poly)phenols industry. Dietary supplements in the form of tasteless capsules are also appreciated in North America and Asia-Pacific. (Transparency Market Research, 2017)

Different types of plant materials, such as crop wastes and residues, provide high quantities of these beneficial compounds. However, every year thousands of tons of crops wastes are generated in Europe without any substantial use from producers or agrofood-industry sector.

At the moment hazelnut skin (ca. 2% of hazelnut seed weight), residual biomass of roasting, is usually used as animal feed, fertilizer or as raw material for biogas plants, when it is not landfilled. Due to the high volume-to-weight ratio of skins, storage and transport of the skins are expensive and limit the selection of potential uses to those available in a short geographic range. At present, hazelnut skin is a by-product of hazelnut production and is mainly used by Ferrero for animal feed, thus the economical return is very low.

4.3.4 (Poly)phenols Extraction Process

Extraction of hazelnut skin polyphenolics has been investigated through microwaves, ultrasound, and super-critical CO₂ (Odabaş & Koca, 2016). SWE (Subcritical Water Extraction), also known as Pressurized Liquid Extraction, was already applied to natural compounds, and more specifically to the flavonoids extraction, but the extraction of hazelnut skin by SWE is not well described. Indeed, only one recent study describes the efficiency of subcritical extraction of (poly)phenols from hazelnut skin (Büyükkileci & Sürek, 2018). Compared to conventional techniques of simple extraction with water, SWE permits to avoid organic solvents and reduces the amount of water used in the process.

To perform SWE, a discontinuous and static extraction is mentioned in literature; it is known as ASE (Accelerate Solvent Extraction) technology and was published in 2017 by the company Activ'Inside together with the University of Toulouse, France (Moras, Rey, Vilarem, & Pontalier, 2017). The extraction of flavan-3-ol monomers, such as catechins, was recently studied from *Arbutus unedo* L. plant roots (Mrabti, Jaradat, Fichtali, Ouedrhiri, Jodeh, Ayesh, et al., 2018). This promising eco-friendly alternative technique is now suitable on small pilot plant (5L to 10L) scale. Compared to acetone and methanol extraction, a recent study showed higher yields with SWE in a high pressure system of 600 mL stainless steel high pressure reactor (35 g of raw material treated) (Büyükkileci & Sürek, 2018).

The aim of the current Hazelnut project is to optimise such a trustworthy alternative technology for the extraction of valuable co-products from hazelnut skin. The strategy is chosen to limit the environmental impact and to produce “clean” food grade ingredients. Compared to conventional solvent extraction, this process will respect the principles of green chemistry as much as possible and should be able to produce different extracts with high content of (poly)phenols tailored to human nutrition, cosmetics and the feed industry.

According to one of the Ferrero partners, the extraction of flavan-3-ols through a 10L SWE pilot plant was already performed on preliminary tests. The efficiency of the method was followed by HPLC-FLD (Robbins, Leonczak, Johnson, Li, Kwik-Urbe, Prior, et al., 2009) in order to separate and quantify flavan-3-ols fractions from monomers to decamers.

Those preliminary data indicate that the final extract obtained from hazelnut skins by this 10L SWE pilot plant contains more than 5% of flavan-ols monomers, oligomers and polymers, on dry matter. The proportions of monomers and oligomers were respectively 17.56% and 32.64%. Therefore, SWE seems an interesting and validated approach to extract flavan-3-ols fraction without organic solvent from hazelnut skins. Considering that, according to a HPLC screening study (Del Rio, Calani, Dall'Asta, & Brighenti, 2011), native hazelnut skin contains an average of 0.67% of (poly)phenols, the SWE allows to increase more than 7 times the concentration of flavan-3-ols without purification. Indeed, batch and static SWE of hazelnut skin extraction at pilot scale and plant scale can be considered as a major development axis of the project. Further optimization and modelling will permit to increase the purity and recovery yield of the extract.

Finally, SWE could be studied in continuous system as a further application. Twin-screw extruder could be used as a dynamic continuous reactor with high thermo-physical constraints. The Laboratory of Agro-chemistry, University of Toulouse, has been developed in recent years an expertise in twin-screw extruder extraction. Recent studies have already demonstrated the capacity of this technology to extract (poly)phenols from complex plant matrix (Celhay, Mathieu, Candy, Vilarem, & Rigal, 2014). The existing twin-screw extruder pilot plant at the Laboratory of Agro-Industrial Chemistry facility will permit to study the continuous extraction of (poly)phenols from hazelnut with 15 to 75 kg/h treatment rate.

In order to increase the final concentration of (poly)phenols, a downstream process of membrane filtrations (UF/NF) is suitable for purifying flavanols from plant extract (Santamaría, Salazar, Beltrán, & Cabezas, 2002). Different membrane cut-offs were identified from the literature: 500 KDa to 1000 KDa and 4 KDa to 200 KDa. These technologies will be applied and dimensioned for application to the SWE extraction treatment. Once raw material (hazelnut skin) characterization and definition of an analytical method suitable for process monitoring, the methodology envisaged is to optimize and model the SWE on a 10L pilot. The next step is therefore to define the parameters and constraints necessary for hazelnut skin extraction in order to design a larger, pre-industrial, demo SWE tool.

The industrial-scaled application will then be transferred and studied on a larger pilot plant (100L to 200L). To this purpose, an industrial demonstration pilot already exists for continuous process. The study will thus focus on a small pilot and then on a larger pilot plant capable of processing up

to higher amount of raw material. Batch and continuous SWE of hazelnut skin will be optimized and integrated in a complete production line, including known purification and drying methods.

The final products should be developed taking into account specific needs, possibility to select components or different mix of polyphenols allow a range of potential high quality products containing hazelnut skin extract as a source of biologically active compounds able to improve human health, and supported with scientific facts. The collaboration with well-established companies and research centres will be key for the cosmetic and animal market. Last, this strategy could pave the way for the revalorisation of other hazelnut by-products.

4.3.5 (Poly)phenols from Hazelnut Skin: Opportunity for Ferrero

Hazelnut skin has been now deeply characterized for its (poly)phenolic profile, which comprises mainly flavan-3-ol monomers (catechins) and oligomers (condensed tannins or proanthocyanidins) (Del Rio et al., 2011). These subclasses of (poly)phenols or phenolic compounds are well-known for their biological properties and their contribution to the prevention of non-communicable diseases (Ottaviani et al., 2018, González-Sarrías et al., 2017, Schroeter et al., 2010, Osakabe and Terao, 2018, Borges et al., 2017, Dower et al., 2016, Clifford et al., 2013). This makes hazelnut (poly)phenols a valuable source of bioactive compounds with multiple potential applications in different marketplaces. To date, the market of (poly)phenol extracts offers a growing, dynamic environment to develop new products from selected sources rich in (poly)phenols (Transparency Research Market, 2017, Allied Market Research, 2017). In this sense, preliminary research underlines the health prospects of hazelnut skin (poly)phenols (Caimari et al., 2015). Moreover, a recent pilot study carried out by one of the Ferrero partners in a small group of volunteers (Mocciaro et al., 2019) has shown that a drink rich in hazelnut skin (poly)phenols extract, in comparison to a placebo drink, was able to improve significantly some markers of endothelial function when participants were classified as high-producers and low-producers of specific phenolic metabolites. A thorough analysis of the urinary excretion of phenolic metabolites showed that the hazelnut skin (poly)phenols were highly bioavailable. Overall, this study demonstrated that hazelnut skin (poly)phenols, supplemented as an extract drink, are bioavailable and show potential beneficial effects, although with individual differences. However, further investigation on hazelnut skin (poly)phenols is needed before claiming with a proper scientific background that new hazelnut

polyphenol-rich extracts or dietary supplements are able to impact human health. That's why the bioavailability of hazelnut skin (poly)phenols, consumed through new and concentrated formulations, needs to be comprehensively assessed looking at the ADME (absorption, distribution, metabolism, excretion) as well as putatively assigning biological effects.

The further step of this research will require detailed studies of the bioavailability of hazelnut skin (poly)phenols in humans, taking into account for the first time novel formulations of dietary supplements. The quantification of both phase II conjugates of flavan-3-ols and phenolic metabolites of colonic origin, like phenyl- γ -valerolactones, will also be considered, since these microbial-derived metabolites represent the main compounds in circulation upon consumption of flavan-3-ol-rich sources (Del Rio et al., 2010, Castello et al., 2018). Moreover, the bioavailability, metabolism, and pharmacokinetic profile of hazelnut skin (poly)phenols will be assessed in comparison to other recognised, commercially-available sources of similar types of flavan-3-ols, such as cocoa, grape seed, and cranberry extracts. This comparison with other sources of flavan-3-ols will favour a better understanding of the bioavailability of hazelnut skin (poly)phenols and will endow this by-product with a more robust evidence, a valuable asset when applying for health claims already approved for other sources of flavan-3-ols, such as cocoa (EFSA, 2014). Finally, all the human interventions with hazelnut skin (poly)phenols aiming at providing the scientific background required for an EFSA positive scientific opinion on a dietary supplement, will be backed by a comprehensive analysis of the phenolic metabolites in circulation. This will provide the link between biological effect and presence of bioactive compounds in the circulatory system.

In addition, the colonic metabolism of hazelnut skins (poly)phenols has been a topic deeply investigated by the University of Parma in the past years (e.g. Calani et al. 2012,). At the same time, the stability of hazelnut skin phenolic compounds during storage and the cytotoxicity and genotoxicity of a hazelnut skin extract-based drink were studied by the University of Parma (2015-2016). Results accounted for the high stability of the phenolic composition of hazelnut skin extracts and drinks during storage. In addition, hazelnut skin (poly)phenols did not show cytotoxic or genotoxic effects, as assessed in different cell lines and in standard toxicity test in animals. These results support the prospects of hazelnut skin extracts for further technological developments.

4.3.6 Dietary Supplement

The use of hazelnuts in Agri-food industries produces tons of by-products, like hazelnut skin. This product is far from being a valueless raw material. Indeed, hazelnut skin is rich in monomeric and oligomeric flavanols (Del Rio et al. 2011), a class of (poly)phenols recognized for their beneficial effects on cardiovascular and cognitive functions, and could constitute a valuable food supplement for the nutraceuticals market. There is huge demand on brain health supplement, valued at USD 2.3 billion in 2015 and expected to reach USD 11.6 billion in 2024. In addition, the market for cardiovascular health is of USD 2.4 billion at the moment. According to the World Health organization, 47.5 million of persons are diagnosed for mental health problems and each year 17.7 million of deaths are directly related to cardiovascular disease (CVD). These diseases represent important cost for the society (e.g. USD 885 billion for treatment of dementia). Currently, they are treated using pharmaceutical approaches usually associated with moderate efficacy and serious side effects. For this reason, it is urgent to develop new, natural and innovative approaches to prevent cardiovascular and cognitive diseases.

Cardiovascular disease (CVD) represents the most common cause of death worldwide. The consumption of natural polyphenol-rich foods has been related to a reduced risk of CVDs, including coronary heart disease and stroke. Intervention studies strongly suggest that flavan-3-ols from cocoa exert a beneficial impact on cardiovascular health, through the improvement of vascular function. Several potential mechanisms are supposed to be involved in the positive effect of cocoa; among them activation of nitric oxide (NO) synthase, increased bioavailability of NO as well as antioxidants, and anti-inflammatory properties.

Impaired vascular health also bears a significant role in the development of cognitive dysfunction and dementia (Sahathevan, Brodtmann, and Donnan 2012). Reduction of CVD risk factors could potentially be associated with a reduction of cognitive impairment. Indeed cerebral blood flow (CBF) has been related to cognitive functions and local CBF reduction can cause hypoxia, consequently accelerating cognitive decline (Catchlove et al. 2018). The cognitive performance depends on the collaboration between vascular cells and neurons. Normal neurovascular coupling ensures the continuous brain's blood supply via the tight control of CBF in order to deliver appropriate oxygen levels to neurons and remove toxic by-products (Gorelick, Scuteri, and Black

2011). It has been demonstrated that the regulation of global blood flow affects the response of regional CBF to neural coupling and potentially affects cognitive performance in pathological and non-pathological conditions (Ogoh 2017). Peripheral systemic vascular markers, like endothelial function reactivity, are possible proxy for detection of cerebral blood flow dysfunction (Prakash et al. 2016). In the light of these results, developing solutions to improve vascular health expressly targeting endothelial function could be a smart strategy in promoting brain activity and preventing cognitive alterations.

Several epidemiological studies have shown positive associations between the intake of flavonoids, a subclass of (poly)phenols including flavan-3-ols, and memory during ageing-related cognitive decline (Letenneur et al. 2007; Devore et al. 2012; Kesse-Guyot et al. 2012; Lefèvre-Arbogast et al. 2018). Moreover, interventional randomized clinical trials have demonstrated that daily supplementation with flavonoids, especially monomers and oligomers, ameliorates both cognition (Field, Williams, and Butler 2011; Krikorian et al. 2012; Bensalem, Dudonné, Etchamendy, et al. 2018) and endothelial function (Barona et al. 2012).

Concomitantly with a CBF increase in learning and memory-associated brain structures (assessed by functional Magnetic Resonance Imaging), improvements of cognitive performances were measured on a spatial recognition task in healthy older adults after a three months supplementation with flavonoid-rich cocoa extract (Brickman et al. 2014; Lamport et al. 2015). These demonstrations suggest that flavanols-rich foods, especially monomeric and oligomeric, have an acute effect on cognition related to the improvement of cerebral blood flow (Lamport et al. 2014). Supporting this hypothesis, two acute studies have also shown consistent potential beneficial effects of cocoa flavanols consumption on working memory and attention in younger subjects (Field, Williams, and Butler 2011; Scholey et al. 2010).

In the context of the present project on hazelnut skin, it is of particular interest to draw a parallel with the evidence already collected on the beneficial effect of flavan-3-ol-rich cocoa extracts, especially monomers and oligomers. In fact, for the latter source of flavanols, a health claim on “*maintenance of normal endothelial health*” has been positively evaluated by the European Food Safety Authority (EFSA) and authorized by the European Commission.

Hazelnut skin is rich in (poly)phenols, particularly in monomeric and oligomeric flavanols which account for 95% of the total polyphenol, as demonstrated by one of the project partner using

conventional aqueous extraction methods (Del Rio et al. 2011). Furthermore, recently one of the consortium partners made preliminary experiments on hazelnut skin raw material using a lab scale subcritical water extraction process and obtained a flavanol monomer and oligomer rich extract with a profile comparable to the cocoa ones used for the EFSA Health claim demonstration (Table below).

*Table 2 Comparison between flavanols composition of cocoa extract and hazelnut skin extract obtain by a partner from the Consortium during recent preliminary experiments with subcritical water extraction.
 FONTE: Ottaviani et al. 2012*

	Monomers	Oligomers		
	DP1	DP2	DP3	DP>3
Cocoa extract	17,4%	15%	1,6%	66%
Hazelnut extract	17,6%	18,9%	8,2%	55,3%

Considering the content in polyphenolic bioactives of hazelnut skin and the clinical evidences described earlier, the extract produced during the present project will be particularly suited for use as a food supplement for both vascular and cognitive health applications.

Before applying for EFSA health claims on vascular health and cognition, it will be necessary to get evidence from at least two independent randomized clinical trials per application. Indeed, all claims need to be scientifically assessed by a panel of experts in order to ensure efficacy and protect consumers. That is why, during this project, all studies will be carried out in the strict respect of gold standard procedures for clinical research, supported by the most updated scientific evidence in the field, and in line with EFSA recommendations. Obtaining in the future an EFSA claim approved for hazelnut's (poly)phenols extracts would have highly positive impact on the product marketing.

4.3.7 Animal Feeding – Ruminants

Hazelnut by-products might represent a potential interesting nutritive supplement for ruminants as well. Hazelnut skin is rich in crude fat (more than 20% DM) and fibres (about 40-50% DM) (Cetinkaya and Kuleyin, 2016). Hazelnut by-products contain also high amounts of secondary compounds, especially phenolics, condensed tannins and vitamins (Goncuoglu Tas and Gokmen, 2015, Masullo et al., 2017, Quijada et al., 2018). These compounds are likely to improve animal performance and health, while decreasing nitrogen and methane wastes and improving the quality of milk and dairy products.

Shahidi et al. (2007) reported that hazelnut by-products are an excellent source of natural antioxidants, which are essential in animal nutrition to reduce the effects of oxidative stress in ruminants. Dietary condensed tannins and phenolics are known to decrease ruminal methanogenesis, thus mitigating greenhouse methane emissions (Jayanegara et al., 2012). This could represent a high environmental benefit considering that ruminants are the major contributor to methane emission worldwide. Condensed tannins and phenolics also affect the degradation of proteins into the rumen, thus increasing nitrogen efficiency of diets and reducing nitrogen losses in the environment (Patra and Saxena, 2011). These positive effects were previously observed *in vitro* when hazelnut skins were added to a hay-based diet for ruminants (Niderkorn et al., 2018). The fat fraction of hazelnut skin was found to contain very high amounts of tocopherols and oleic acid (Ozdemir et al., 2014) that are two desirable compounds for improving the nutritional and organoleptic qualities as well as shelf life of milk and dairy products.

Therefore, a large body of evidence suggest, and already partially sustain, the multiple benefits of hazelnut by-products for ruminant nutrition.

A first *in vivo* experiment made in 2017 by the University of Turin (personal communication) assessed the potential interest for hazelnut skins used as feed ingredient for dairy cows. Animal performance and milk quality parameters, including the possible occurrence of unforeseen effects like low palatability of the ration, production losses, and side effects, were monitored in an experimental farm in response to a daily consumption of 1 kg/cow/day of toasted hazelnut skins. No negative effects on the performances and on the quality of milk (proteins and sensory attributes) were found while a positive effect on milk fatty acid profile (namely, an increase of oleic acid) was

shown. However, no anti-inflammatory response following hazelnut skin feeding could be appreciated. These first promising results must be confirmed by broader investigations that should take into account also animal health aspects, as well as monitoring the possible reduction of gaseous emissions linked to modified ruminal metabolism.

Hazelnut skin, thanks to its high content in saponines and tannins, may also be used as primary component in formulated feed additives for farmers. The use of these feed additives made of natural ingredients and incorporated in the animal diet at low quantities (from 20 to 50 g/day/animal) is a fast-growing sector in the animal feed industry. Several plants or extracts have already been tested *in vitro* with the aim to reduce methane and ammonia emissions. Saponines and tannins are currently the most recognized molecules with a favourable activity on reducing methanogenesis. Most of tannins currently used in animal production are from South America plants such as *Schinopsis lorentzii* (Quebracho) or *Leucaena leucocephala*. The hazelnut tannins/(poly)phenols are interesting ingredients to produce standardized blends (based on phenol actives) in order to reinforce the final product in claiming methane reduction and/or proteins savings. The activity of these blends has now to be validated *in vivo*.

As a summary, despite the promising effect of hazelnut skin (poly)phenols, large-scale *in vivo* studies remain scarce and are required to validate the potential interest of hazelnut by-products for ruminant feeding.

4.3.8 Animal Feeding – Pet Food

In addition to their strong antioxidant capacities, flavanols monomers and oligomers have been recognised for their beneficial effects on cardiovascular and cognitive function not only in humans but also in dogs (Fragua et al. 2017). Hence, extract generated from hazelnut skin could constitute an efficient additive with health-care application for the dog feeding market. Therefore, in the present project, the impact of a supplementation on endothelial function and global health of dog will be evaluated. Importantly, one of Ferrero's partners has already obtained preliminary results, presented during an international congress of cardiology in 2018 (Moinard and Leray 2018). In this study, made in collaboration with French scientists (veterinary school Oniris, Nantes, France), the

effect of an extract similar to the one intended to be developed from hazelnut skin in term of flavanol monomers and oligomers was assessed on the vascular health in ten dogs. Results demonstrate that an acute supplementation significantly improves endothelial function in dog, as measured by flow-mediated dilation.

Considering that, in the European Union, new feed additives intended for use in animal feeding must obtain a premarketing safety authorization ((EC) N°1831/2003 and N°429/2008), a parallel safety study in rats will be carried out for the hazelnut skin extract by a GLP-certified CRO. This toxicological study will identify the product's lowest No Observed Adverse Effect Level (NOAEL), in accordance to requirements from EFSA and Organization for Economic Cooperation and Development. The final target will be to obtain a European Feed Additive approval to promote the patented extract.

4.3.9 Cosmetic Sector

Plant-derived ingredients were among the very first cosmetics. Natural colorants, plant juices for soothing and protection from insect pests, and fragrant oils were known and used in ancient times. Although there has always been interest in the use of ingredients derived from plants in cosmetics, that interest exploded beginning in the 1990s, with new discoveries of benefits, greater standardization and control of raw materials, and new formulation techniques. Based upon the historical experience with botanical ingredients, knowledge on their safe use has been gained. However, manufacturers of cosmetic and personal care products are required by law to adequately substantiate the safety of their products, especially for novel ingredients/formulations.

The use of hazelnut and its derivatives is not widespread in cosmetics, although some companies started offering products with hazelnut derivatives within their components. In the past five years, 1,600 products containing ingredients derived from hazelnuts have been launched worldwide (Mintel's GNPD database Global New Product Data for: *Corylus Avellana Bud Extract*, *Corylus Americana Seed Extract*, *Corylus Avellana Seed Extract*, *Corylus Avellana Flower Extract*, *Corylus Avellana Leaf Extract*, *Corylus Americana Seed Oil*, *Hydrogenated Hazelnut Oil*, *Hydrolyzed Hazelnut Protein*, *Corylus Avellana Seed Oil*, *Corylus Avellana Shell Powder*).

Among the potential ingredients that may derive from hazelnut by-products, skins and shells, two possible “trends” can be identified in order to add value at the raw materials:

- Fibres, actually used in cosmetic as bulk agent for mascara or scrubs

Nowadays many types of fibres are used in the cosmetic market.

- Polyphenolic extracts attractive ingredients for cosmetics due to their potential biological properties, such as anti-aging activity.

4.4 NUtWAVE Project: Overall Concept

The overall concept of the NUtWAVE project is to demonstrate complete value chains for the by-products of perennial crops across a range of industrial applications. It will therefore consider the factors needed for valorisation of the value chain and for upscaling at each step of the processing. This approach ensures that the value chains will remain balanced by simultaneously considering all constituent steps: increasing production of affordable high-quality biomass, whilst creating a market pull on the demand side by increasing and further developing the valorisation options. It will therefore integrate the potential provided by novel supply options with the security of industry demand.

Environmental, social and economic aspects are integral part of the project concept, from the involvement of regional associations directly connected with farmers - which will have significant social and economic benefits (creation of jobs, restoration of unproductive by-products) - to the final users of functional ingredients. Through this project we'll demonstrate and validate the sustainability and suitability of new end-products through the extraction of new added value products (fibres and (poly)phenols) from hazelnuts by-products.

The NUtWAVE project is fully aligned with the objectives and work plan set up by the BBI JU, since the project will contribute to development of more resource-efficient and sustainable value chains, thereby contributing to build a practical example of circular economy.

The next part will explain how the Nut-WAVE project could fit into a European scale-up project, with the positive impacts that this project may have on added values among the supply chain in reducing environmental impact, improving the management of renewable resources and by involving different sectors to obtain benefits from bio-waste.

4.4.1 Methodology

The NUt-WAVE project is a demonstration-scale 5-year project with eleven partners from five countries. It considers elements across the entire value chain, and combines demonstration activities with underpinning research activities. The focal point of the project is setting up demonstration cases. These demonstration cases are accompanied by research activities, whose aims are to validate the environmental and socio-economic impact of the new value chains envisaged.

NUt-WAVE will undertake a holistic and circular approach of hazelnut value chain from “farm-to-farm”, including crop production, hazelnut processing and application for several industrial sectors. In fact, it will address a wide range of valorisation pathways in different industries (cosmetics, animal feeding, functional food, packaging, dietary supplement). Finally, it will close the loop, with the possible use of biochar as fertilizer in the farm sector of whatever residual remains.

4.4.2 Expected Impacts

The NUt-WAVE project will contribute to the EU Bio-economy by adding value to by-products from the processing of products from the perennial crop *Corylus avellana* and will open the way for wider applications of the demonstrated technologies to other side-streams from food industry. The project will also contribute to the horizontal cross-cutting priority to promote Key Enabling Technologies. With the participation of various actors of the value chain, new technological solutions and products will be developed. The new production methods and innovative uses of the extracted bio-active compounds in food, feed, cosmetics and packaging materials bear the potential

to create new advanced processing approaches that will ultimately contribute to EU's production of high-value added products. The use of food industry by-products as raw materials has an enormous potential to add value to the society and to reduce the environmental impact, thus allowing improved management of renewable biological resources. The rationale proposed by NUt-WAVE project could be replicated in other sectors where production and processing of nuts and large amount of lignocellulosic by-products are present. Since the ingredients obtained from NUt-WAVE could find a variety of applications, particularly as ingredients of functional foods, but also as supplements and nutraceuticals, animal feeding and cosmetic sectors, NUt-WAVE project will contribute to the creation of new markets, achieving high impact on the hazelnut value chain.

Current commercial processes are based on lab and pilot equipment. Therefore the NUt-WAVE project will include larger scale demonstration actions and will explore the feasibility of extraction of (poly)phenols and high-value fibre from hazelnut shells and skin for future upscaling. The performance indicator for this objective is the successful establishment of the demonstration scale trials.

4.4.2.1 BBI KPI 1: Create at least one new cross-sector interconnection in bio-based economy

The NUt-WAVE project will generate multiple, new cross-sector interconnections through the participation of partners that are not traditionally directly involved. The production of dietary supplements using bioactive compounds from hazelnuts brings together actors from the health industry and food industry in collaboration for creating products with highly interesting health claims. The collaboration will create the ground for cross-fertilisation and exchange of stakeholder knowledge. As an example, cosmetic industry has traditionally sourced ingredients from other partners than food industry. In this project, the food industry and cosmetics are forging a collaboration to develop new uses for bioactive ingredients to fulfil the market demand for natural products with bioactive properties.

4.4.2.2 BBI KPI 2: Set the basis for at least one new bio-based value chain

The NUt-WAVE project, with the involvement of the project partners and their commercial operations, will develop and demonstrate the operation of three distinct value chains using hazelnut skin:

1. Production of dietary supplements rich in (poly)phenols.

The extraction of bioactive compounds will be followed by the formulation and testing of dietary supplements with industry and research partners specialised in the health sector. The placing on the market of such products will be envisaged through normal distribution networks of the responsible partner.

2. Animal feed or additive with bioactive properties (antioxidant, antimicrobial...) and improving animal performances.

The project will test both feed products for ruminants, in collaboration with the farming sector, and feed products for pets, in collaboration with feed industry partners, to establish their functional properties and antimicrobial function for better animal health.

3. Cosmetic products with bio-active ingredients: skin care product with (poly)phenols and make-up product with fibre.

The food industry partners, supporting the extraction of bioactive compounds, will collaborate with a specialised cosmetics company to produce, test and envisage placing of the market of new cosmetic products.

4.4.2.3 BBI KPI 3: Create at least two new demonstrated consumer products based on bio-based chemicals and materials that meet market requirements

The project will develop a range of products using the bioactive compounds obtained from hazelnut by-products. Compounds and products will be evaluated and documented to meet all regulatory requirements and market standards:

1. Dietary supplements

The consumer products developed will consist in a new dietary supplement from hazelnut skin extracts, rich in bioactive flavan-3-ols. For this product, the project will produce the scientific evidence needed to obtain EFSA health claims approval on two different beneficial physiological effects for the general healthy adult population: vascular function maintenance and cognitive function improvement. In addition, the product's effect on microbiota composition and its prebiotic effect will be evaluated.

2. Feeds or additive for animal farming with bioactive properties (antioxidant, antimicrobial...) improving animal health and performances

Different hazelnut by-products will be tested as feed or additives in ruminants' nutrition with the farming partners in the project. Hazelnut by-products have interesting properties that could be exploited to reinforce animal health, improve production efficiency and product qualities and mitigate methane emissions. Farm testing will make it possible to investigate the potential use of such products in alternative prophylactic strategies able to stimulate immune response and to limit use of antibiotics at farm level.

3. Pet food rich in (poly)phenols

Pet food products aimed to vascular function improvement and global health maintenance in dogs will be developed and tested. During the evaluation, the animal global health will be assessed by objective observation and plasma samples will be collected and analysed for identifying biological response and mechanisms of action. A global composite score, taking into account the various parameters followed (endothelial function, biological data, coat aspect), will be calculated in order to better express a global improvement of health status.

4. Skin care cosmetic products with (poly)phenols and Make-up cosmetic products with fibre

Innovative cosmetics containing ingredients derived from hazelnut by-products will be developed by the cosmetic partners. In the cosmetic industry, there is an increasing demand for products based on natural ingredients (scrubs, mascara, eyeliner, kajal, back injected powders, lipsticks and lip-glosses). These products will be formulated and tested to comply with the requirements of the Regulation EU 1223/2009.

4.4.2.4 BBI KPI 4 Obtain at least 20 % more value from the used new/alternative feedstock than state-of-the-art methods.

Currently the value of the residual biomass obtained from the primary processing of hazelnuts is very low. As previously mentioned, current uses include burning, use as feed, fertiliser or in biogas fermentation processes. Through the various alternative uses of these residuals implemented by the project, it is expected that the value of the feedstock will be increased by more than 20%. The economic assessment foreseen in the project will evaluate and confirm the positive economic impact of the valorisation of biomass through a circular economy approach.

5. Conclusions

This thesis demonstrates that Confectionary Industry could evolve their business model in line with the new European requirements in terms of sustainability, with benefits on the whole system. Such a new business model is driven by consumer's needs and supported by well-oriented research. With the high volumes of bio-waste generated by the raw material used - i.e. the hazelnut - Ferrero is not only part of the fight against a potential environmental problem but also against the economic burden of their management and disposal, which represents a relevant additional cost. However, by exploiting the hazelnut by-products, I intend to demonstrate that there is a huge potential in extracting bioactive ingredients able to grant competitive advantages and to fit into the Ferrero's core business, but also to new innovative sectors

This business model based on hazelnut supply chain not only meets the desires of the European Commission in terms of sustainable industry but also allows the recovery of bio-waste derived ingredients with high commercial values.

This thesis shows the feasibility of cost-effective and sustainable exploitation of the hazelnut biomass through a circular economy approach. The value of the biomass is increasing through the extraction from waste streams and valorisation of bioactive and functional ingredients to be used in consumer products for dietary supplements, food, animal feeding and cosmetics.

Finally, this thesis shows that well designed, multi-stakeholder projects may be proposed under the current EU framework programs to implement this circular economy approach and integrate the sustainability principles in business models of different industrial and agricultural sectors along the hazelnut value chain.

5.1 Relevant Social, Sustainability and Health Impacts

In line with my position of Ferrero project manager for the BBI call, this thesis does not only cover the part of the hazelnut biomass that is used for food production. Responding to the challenges set in the said call, the thesis is instead focused on the bio-waste streams derived from the processing of the hazelnut crop.

The project, that constitutes the main activity of my doctoral work, addresses all the socio-economic and environmental challenges of the hazelnut value chain. The improvements in the logistics of collection and primary processing of hazelnuts will affect the rural hazelnut-producing communities by providing improved and more sustainable production technologies and the opportunity to better valorise their product. The social impact will be enhanced by knowledge transfer and support for social innovation initiatives. In the down-stream processing phase, the project addresses environmental aspects, such as reducing the waste pressure of the industrial use and providing alternatives to the environmentally harmful use of the by-products such as burning.

The project will have also an impact on quality of life and human health. The (poly)phenols and fibre extracted from hazelnut skin have the potential to improve the consumer health condition. In the case of the hazelnut skin extract, dietary supplement rich in bioactive flavan-3-ols, the project will investigate two different beneficial physiological effects on the health of adult population: vascular function maintenance and cognitive function improvement. In addition, the product's effect on microbiota composition will be evaluated.

Another positive impact will be on animal health and performance. Feed that use as additives bioactive extracts or hazelnut by-products might have interesting properties to reinforce animal health, improve production efficiency and quality and mitigate methane emissions. In addition, bioactive compounds such as (poly)phenols or tannins from hazelnuts (antimicrobial and antioxidant properties) have the potential to be used in prophylactic strategies to stimulate animal immune response and limit the use of antibiotics.

5.2 New Market Opportunity for EU Companies

The range of products developed by the NUt-WAVE project will become a reference of multiple opportunities for EU companies using bioactive compounds derived from biomass by-products. Demonstration of the positive benefits on health of fibre-enriched or (poly)phenol-enriched food products will open new opportunities for the entire EU food sector. Not only this approach will be able to answer the demand on the EU market for products carrying health benefits, such as body

weight management and gastrointestinal health, but also it will have the opportunity to further spread into the global extra-European market.

The use of (poly)phenols and tannins from hazelnut, as an alternative prophylactic strategy to reduce infections and mitigate the use of antibiotics in animals, might create again huge market opportunities for a range of EU companies. Partners in the project will have the opportunity to develop and test promising products for an ever-increasing market for feed and pet food.

Use of plant extracts in cosmetic products has been a trend in the industry for a while. The properties of hazelnut extracts will allow the development of a range of products able to answer to new consumer request. Fibre extracted from hazelnut shells is an innovative natural ingredient for cosmetic products, and can be used as bulk agent for skin care products for which the European market amounts to 800 M€. The (poly)phenols from hazelnut skin can be incorporated in products with antioxidants and anti-aging properties.

5.3 Contribution to Other Important Impacts (environment, social, SMEs)

A key element of circular- and bio-economy is to put emphasis on the reduction of environmental impact, recycling, energy efficiency, production of biodegradable products with minimal residual waste to dispose and a huge added value. Among the main future challenges for bio-economy, one is the production of biomass without environmental over-exploitation as well as its better use, including the reduction of residues and waste. Increasing use of by-products will have a positive impact on supply, both directly and indirectly. Direct benefits are related to reduce need for newly grown biomass. Indirect benefits are that the use of by-products might have an impact on the initial price. Indeed, under some circumstances, the farmer or the food industry may get a better price when more added value is recovered from the goods grown or transformed. This may create a positive cycle: more investments, higher yields, more efficient land-use, less environmental degradation and lower costs. My thesis shows that the NUt-WAVE project has the potential to generate a positive social impact and help farmers to enhance their role as provider of raw by-products biomass and help increasing their value generation.

The NUt-WAVE project will develop and test good practices by fostering protocols and technologies for by-product-derived new ingredients. It will of course focus on hazelnut but will indirectly contribute to improve the environmental and economic sustainability of other food commodities and food processing sectors. Sustainable products have difficulties in entering the market partly because of price differences. Developing alternative sources for valuable bioactive compounds such as (poly)phenols and fibres will increase market opportunities to develop new products using such ingredients. Consequently, this will lead to market development, stimulating innovation beyond niche markets. It will open the door for SMEs and other actors to take advantage of new market opportunities.

5.4 Barriers and Guidance

The legislation framework limits the generalizability of the results. A favourable and stable regulatory environment surely can help innovation in the food and supplement sector. The future development of the market for bio-based products needs a stable and long-term political support. Considering the dependence on regulation-induced demand, an important issue raised by business experts is the presence of a supportive and stable regulatory framework.

Growth and development of the bio-economy is policy-driven, and therefore depends on suitable legislation and regulation. Changes in regulation could therefore have a direct effect on the framework in which the NutWAVE project operates, thus influencing its expected impacts. The regulation could change due to food safety concerns as well as animal feed safety issues, and the growth of the bio economy sector and adaptation of novel value-chains might be hindered by an overburden of regulatory issues. However, strategical recommendations may be enforced to inform policy-makers of scientific developments, allowing them to regulate in a way to minimize the risk of constraining the European bio economy sector, and simultaneously ensuring that food security and environment are protected. As an example, the full exploitation of a novel ingredient, such as AXOS fibre from hazelnut shells, requires that novel food is approved, and it is mandatory that all the evidence is in place for a successful approval of such a novel functional ingredient.

Other prerequisites to valorise the hazelnut by-product and their role in the implementation of new sustainable value chains are proper Life Cycle Assessment and Social Life Cycle assessment analyses.

Consumer acceptance is another barrier. Customers often consider the price of goods at the point of sale not taking into account enhanced nutritional value or their sustainability. The hurdle here to overcome is changing people mind-sets, both of consumer behaviour and of company policies. The consumer will be the actor eventually determining the success of circular economy practices. Thus, it is crucial for the implementation of a circular economy model to drive consumers' willingness to buy products recovered from wastes and to switch, at least in part, from using new products to bio-waste-derived products (Open-BIO, 2015).

Specific consumer research on products obtained from bio-waste is scarce: the attitude towards a product is based on (among others) the perception of the product. A positive perception is a condition for a positive attitude and intention to buy, and further research is needed to help fill this knowledge gap. This will require exploring drivers and barriers to consumers' awareness and acceptance of bio-waste products and what would drive the decision to switch from traditional product to bio-based product in different European countries.

The creation of an official European "bio-based" label would promote the market for bio-based products, bringing also higher level of support for such technologies among industry stakeholders.

Investment in bio-based products may bring important strategic benefits for the Ferrero businesses, such as the positioning as an innovative and technologically-advanced company, and the diversification of supply chains. Other strategic considerations pushing toward this path are the perceived importance of savings in carbon emissions and compliance with environmental regulation as drivers of the future market. Furthermore, the company can benefit from potential subsidies and public incentives and gaining early-mover-advantages, for example in anticipation of future regulations and carbon taxes.

References

- Abdel-Rahman A., Anyangwe N., Carlacci L et al. (2011). The Safety and Regulation of Natural Products Used as Foods and Food Ingredients. *Toxicological Sciences*, Volume 123, Issue 2, October 2011, Pages 333–348.
- Adebooye O.C., (2018). A brief review on emerging trends in global polyphenol research. *Journal of Food Biochemistry*.
- Ahn K. (2017). The worldwide trend of using botanical drugs and strategies for developing global drugs. *BMB Rep*, 50, 111-116.
- ALLIED MARKET RESEARCH. (2017). Polyphenol Market by Product Type (Apples, Green Tea, Grape Seed, and Others) and Application (Functional Beverages, Functional Food, Dietary Supplements, and Others) - Global Opportunity Analysis and Industry Forecast, 2014-2022.
- Anil M. (2007). Using of hazelnut testa as a source of dietary fiber in breadmaking. *Journal of Food Engineering* Volume 80, Issue 1, May, Pages 61-67.
- Barona J., Aristizabal J. C., Blesso C. N. et al. (2012). Grape (poly)phenols Reduce Blood Pressure and Increase Flow-Mediated Vasodilation in Men with Metabolic Syndrome. *J Nutr* 142 (9): 1626–32.
- Barona J., Blesso C.N., Andersen C. J. et al. (2012). Grape Consumption Increases Anti-Inflammatory Markers and Upregulates Peripheral Nitric Oxide Synthase in the Absence of Dyslipidemias in Men with Metabolic Syndrome. *Nutrients* 4 (12): 1945–57.
- Bensalem J., Dudonné S., Etchamendy N. et al. (2018). (Poly)phenols from Grape and Blueberry Improve Episodic Memory in Healthy Elderly with Lower Level of Memory Performance: A Bicentric Double-Blind, Randomized, Placebo-Controlled Clinical Study. *J Gerontol A Biol Sci Med Sci*. 2019 Jun 18;74(7).
- Bensalem J., Servant L., Alfos S. et al. (2016). Dietary Polyphenol Supplementation Prevents Alterations of Spatial Navigation in Middle-Aged Mice. *Frontiers in Behavioral Neuroscience* 10: 9.
- Bensalem, J., Dudonné S., Gaudout D et al. (2018). Polyphenol-Rich Extract from Grape and Blueberry Attenuates Cognitive Decline and Improves Neuronal Function in Aged Mice. *J Nutr Sci*. 2018 May 21;7:e19.

- Bocken N. M., de Pauw I., Bakker C. et al. (2016). Product design and business model strategies for a circular economy. *Journal of Industrial and Production Engineering*, 33(5), 308-320.
- Bolling B. W., Oliver Chen C.Y., McKay D. L. et al. (2011). Tree nut phytochemicals: composition, antioxidant capacity, bioactivity, impact factors. A systematic review of almonds, Brazils, cashews, hazelnuts, macadamias, pecans, pine nuts, pistachios and walnuts. *Nutrition Research Reviews*, 24, 244–275
- Borges G., Ottaviani J. I., Van der Hooft J.J.J. et al. (2017). Absorption, metabolism, distribution and excretion of (-)-epicatechin: A review of recent findings. *Mol Aspects Med*, 61, 18-30.
- Bottone A, Cerulli A, D'Urso G. et al. (2019). Plant Specialized Metabolites in Hazelnut (*Corylus avellana*) Kernel and Byproducts: An Update on Chemistry, Biological Activity, and Analytical Aspects. *Planta Med.* Aug;85(11-12):840-855.
- Brickman A. M., Usman A. Khan, Frank A. Provenzano et al. (2014). Enhancing Dentate Gyrus Function with Dietary Flavanols Improves Cognition in Older Adults. *Nature Neuroscience* 17 (12): 1798–1803.
- Brown R. C., Siew Ling Tey S., Andrew R. Gray A.R. et al. (2015). Association of nut consumption with cardiometabolic risk factors in the 2008/2009 New Zealand adult nutrition survey. *Nutrients* 2015, 7, 7523-7542
- Büyükkileci A. O., & Sürek E. (2018). Extraction of Antioxidant Compounds from Hazelnut Wastes Using Subcritical Water. *Gida / the Journal of Food*, 211-221.
- Caimari A., Puiggròs F., Suárez M. et al. (2015). The intake of a hazelnut skin extract improves the plasma lipid profile and reduces the lithocholic/deoxycholic bile acid faecal ratio, a risk factor for colon cancer, in hamsters fed a high-fat diet. *Food Chemistry*, 167, 138-144.
- Calani L, Dall'Asta M, Derlindati E et al. (2012). Colonic metabolism of (poly)phenols from coffee, green tea, and hazelnut skins. *J Clin Gastroenterol.* 2012 Oct;46 Suppl:S95-9.
- Calani L, Del Rio D, Callegari L. et al. (2012). Updated bioavailability and 48 h excretion profile of flavan-3-ols from green tea in humans. *Int J Food Sci Nutr.* 2012 Aug;63(5):513-21.

- Castello F., Costabile G., Bresciani L et al. (2018). Bioavailability and pharmacokinetic profile of grape pomace phenolic compounds in humans. *Archives of Biochemistry and Biophysics*, 646, 1-9.
- Catchlove S. J., Macpherson H., Hughes M. E. et al. (2018). An Investigation of Cerebral Oxygen Utilization, Blood Flow and Cognition in Healthy Aging. *PLoS ONE* 13 (5): 1–21.
- Celhay C., Mathieu C. E., Candy, L. et al. (2014). Aqueous extraction of (poly)phenols and antiradicals from wood by-products by a twin-screw extractor: Feasibility study. *Comptes Rendus Chimie*, 17(3), 204-211.
- Cesarettin A., Joana S.A. and Fereidoon S. (2006). Functional Lipid Characteristics of Turkish Tombul Hazelnut (*Corylus avellana* L.). *J. Agric. Food Chem.*, 54, 10177-10183
- Cetinkaya N., Kuleyin Y.S. (2016). Evaluation of Hazelnut hulls as an alternative forage resource for ruminants animals. *International Journal of Agricultural and Biosystems Engineering*, 10, 319-322.
- Chen C.Y., Milbury P.E., Lapsley K. et al. (2005). Flavonoids from almond skins are bioavailable and act synergistically with vitamins C and E to enhance hamster and human LDL resistance to oxidation.
- Clifford M. N., Van der Hooft, J. J. J. and Crozier, A. (2013). Human studies on the absorption, distribution, metabolism, and excretion of tea (poly)phenols 1-3. *American Journal of Clinical Nutrition*, 98, 1619S-1630S.
- Cristofori, V. (2005) Fattori di qualità della nocciola. PhD thesis, University of Tuscia, Viterbo
- Crozier A, Jaganath IB, Clifford MN. (2009). Dietary phenolics: chemistry, bioavailability and effects on health. *Nat Prod Rep*. Aug;26(8):1001-43.
- Curti C., Brindani N., Battistini L., Sartori A. (2015). Catalytic, Enantioselective Vinylogous Mukaiyama Aldol Reaction of Furan- Based Dienoxy Silanes: A Chemodivergent Approach to γ - Valerolactone Flavan- 3- ol Metabolites and δ - Lactone Analogues. *Advanced Synthesis & Catalysis* 357.18 (2015): 4082-4092.
- Davidi A., Reynolds J., Njike V.Y. et al. (2011). The effect of the addition of daily fruit and nut bars to diet on weight, and cardiac risk profile, in overweight adults. *J Hum Nutr Diet*. Dec;24(6):543-51.

- Davis P. A., Jenab M., Vanden Heuvel J. P. et al. (2007). Tree Nut and Peanut Consumption in Relation to Chronic and Metabolic Diseases Including Allergy. *The Journal of Nutrition - 2007 Nuts and Health Symposium*.
- Del Bo' C., Bernardi S., Marino M. et al. (2019) Systematic Review on Polyphenol Intake and Health Outcomes: Is there Sufficient Evidence to Define a Health-Promoting Polyphenol-Rich Dietary Pattern? *Nutrients*, 11, 1355.
- Del Rio D., Calani L., Cordero C. et al. (2010). Bioavailability and catabolism of green tea flavan-3-ols in humans. *Nutrition*, 26, 1110-1116.
- Del Rio D., Calani L., Dall'Asta M, Brighenti F. (2011). Polyphenolic composition of hazelnut skin. *J Agric Food Chem*. Sep 28;59(18):9935-41.
- Del Rio D., Rodriguez-Mateos A., Spencer J. P. E. et al. (2013). Dietary (poly) phenolics in human health: Structures, bioavailability, and evidence of protective effects against chronic diseases. *Antioxid Redox Signal*, 18, 1818-1892.
- Demirbas A. (2006). Production and Characterization of Bio-Chars from Biomass via Pyrolysis, *Energy Sources, Part A: Recovery, Utilization, and Environmental Effects*, 28:5, 413-422.
- Devore E. E., Jae H. K., Monique M. B. B. et al. (2012). Dietary Intakes of Berries and Flavonoids in Relation to Cognitive Decline. *Annals of Neurology* 72 (1): 135–43.
- Dower J. I., Geleijnse J. M., Hollman P. C. H. et al. (2016). Dietary epicatechin intake and 25-y risk of cardiovascular mortality: the Zutphen Elderly Study. *The American Journal of Clinical Nutrition*, 104, 58-64.
- EFSA PANEL ON DIETETIC PRODUCTS, NUTRITION, & ALLERGIES. (2014). Scientific Opinion on the modification of the authorization of a health claim related to cocoa flavanols and maintenance of normal endothelium-dependent vasodilation pursuant to Article 13(5) of Regulation (EC) No 1924/2006 following a request in accordance with Article 19 of Regulation (EC) No 1924/2006. *EFSA Journal*, 12, 3654.
- EFSA PANEL ON DIETETIC PRODUCTS, NUTRITION, & ALLERGIES. (2014). Scientific Opinion on the modification of the authorisation of a health claim related to cocoa flavanols and maintenance of normal endothelium-dependent vasodilation pursuant to Article 13(5) of Regulation (EC) No 1924/2006 following a request in accordance with Article 19 of Regulation (EC) No 1924/2006. *EFSA Journal*, 12, 3654.

- Eriksson, M. (2015). Doctoral Thesis - Swedish University of Agricultural Sciences, Uppsala. Supermarket food waste (Acta Universitatis agriculturae Sueciae Vol. 2015, No. 119).
- Estruch R, Ros E, Salas-Salvadó J. et al. (2013) Primary prevention of cardiovascular disease with a Mediterranean diet., *N Engl J Med.* Apr 4;368(14):1279-90 .
- Estruch R., Ros E., Salas-Salvadó J. et al. (2018). Primary prevention of cardiovascular disease with a Mediterranean diet supplemented with extra-virgin olive oil or nuts. *N Engl J Med*; 378:e34
- Faustino M., Veiga M., Sousa P. (2019). Agro-Food Byproducts as a New Source of Natural Food Additives. *Molecules*, 24, 1056
- Ferrero CSR Report 2017.
- Ferrero Hazelnut Company (HCo). (2018). L'origine di un'intuizione e Non solo numeri, ma persone
- Field D. T., Williams C. M., Butler L. T. (2011). Consumption of Cocoa Flavanols Results in an Acute Improvement in Visual and Cognitive Functions. *Physiology and Behavior* 103 (3–4). Elsevier Inc.: 255–60.
- Fischer, G. (2009, June). World food and agriculture to 2030/50. In Technical paper from the Expert Meeting on How to Feed the World in 2050, pp. 24-26.
- Fiskobirlik, (2003). Records of Union Of Agricultural Cooperatives For The Sale Of Hazelnut. Giresun, Turkey, 2003.
- Fite A, Macfarlane GT, Cummings JH, et al (2004) Identification and quantitation of mucosal and faecal desulfovibrios using real time polymerase chain reaction. *Gut*; 53:523-529.
- Foley J. A., Ramankutty N., Brauman K. A et al. (2011). Solutions for a cultivated planet. *Nature*, 478(7369), 337-342.
- Fragua V., Lepoudère A., Leray V. et al. (2017). Effects of Dietary Supplementation with a Mixed Blueberry and Grape Extract on Working Memory in Aged Beagle Dogs. *Journal of Nutritional Science* 6 (35): 1–5.
- Garnett, T. (2013). Food sustainability: problems, perspectives and solutions. *Proceedings of the Nutrition Society*, 72(1), 29-39.

- Geng Y., Fu J., Sarkis J., & Xue B. (2012). Towards a national circular economy indicator system in China: an evaluation and critical analysis. *Journal of Cleaner Production*, 23(1), 216224.
- Geng Y., Sarkis J., Ulgiati S., & Zhang P. (2013). Measuring China's circular economy. *Science*, 339(6127), 1526-1527.
- Ghisellini P., Cialani, C., & Ulgiati, S. (2016). A review on circular economy: the expected transition to a balanced interplay of environmental and economic systems. *Journal of Cleaner Production*, 114, 11-32
- Gidley M.J., Yakubov G.E. (2017). Functional categorisation of dietary fibre in foods: Beyond ‘soluble’ vs ‘insoluble’. *Trends in Food Science & Technology*; Volume 86, Pages 563-568
- Gleick, P. H. (2003). Global freshwater resources: soft-path solutions for the 21st century. *Science*, 302(5650), 1524-1528.
- Goncuoglu Tas N. Gokmen V. (2015). Bioactive compounds in different hazelnut varieties and their skins. *Journal of Food composition and analysis*. 43, 203-208.
- González-Sarriás A., Combet E., Pinto P. et al. (2017). A Systematic Review and Meta-Analysis of the Effects of Flavanol-Containing Tea, Cocoa and Apple Products on Body Composition and Blood Lipids: Exploring the Factors Responsible for Variability in Their Efficacy. *Nutrients*, 9, 746.
- Gorelick Pb, Scuteri A., and Black S. (2011). Contributions to Cognitive Impairment and Dementia a Statement for Healthcare Professionals from the American Heart Association/American Stroke Association. *Stroke* 42 (9): 2672–2713.
- Graedel, T. (1994). Industrial ecology: definition and implementation. *Industrial ecology and global change*, 23-41.
- GRAND VIEW RESEARCH. (2016). *(poly)phenols Market Analysis By Product (Grape Seed, Green Tea, Apple), By Application (Functional Food, Functional Beverages, Dietary Supplements) And Segment Forecasts To 2024*.
- Gustavsson J., Cederberg C., Sonesson U., et al. (2011). Global food losses and food waste (pp. 1-38). Rome: FAO.
- Heiss C., Dejam A., Kleinbongard P. et al. (2003). Vascular Effects of Cocoa Rich in Flavan-3-Ols [6]. *Journal of the American Medical Association* 290 (8): 1030–31.

- Heiss C., Kleinbongard P., Dejam A. (2005). Acute Consumption of Flavanol-Rich Cocoa and the Reversal of Endothelial Dysfunction in Smokers. *J Am Coll Cardiol* 46 (7): 1276–83.
- Hill J. E. (2014). The circular economy: From waste to resource stewardship, part 1. *Proceedings of the Institution of Civil Engineers*, 168(1), 3–13.
http://agri.istat.it/sag_is_pdwout/jsp/Ricerca.jsp (accessed 07/31/2019)
(accessed 08/19/2019)
[https://www.asdreports.com/market-research-report-314134/\(poly\)phenols-market-analysis-product-grape-seed-green-tea-apple-application](https://www.asdreports.com/market-research-report-314134/(poly)phenols-market-analysis-product-grape-seed-green-tea-apple-application) (accessed 08/19/2019)
<https://www.hazelnutcompany.ferrero.com/Ferrero-Hazelnut-Company/> (accessed 07/30/2019)
- Internal data Ferrero 2017.
- Internal Ferrero data, 2015.
- International Tree Nut Council (INC), Geneve, June 15 2002. Official respond to draft report of joint world health organization (WHO) food and agriculture organization (FAO) expert consultation on diet, nutrition and the prevention of chronic diseases. (accessed 07/26/2019)
- ISTAT (Istituto Nazionale di Statistica, Italia). (2017). Consultazione dati coltivazioni legnose - Superfici e produzioni.
- Jakobek L., Matic P. (2019). Non-covalent dietary fiber - Polyphenol interactions and their influence on polyphenol bioaccessibility. *Trends in Food Science & Technology*; Volume 83, Pages 235-247
- Jayanegara A., Leiber F. and Kreuzer M. (2012). Meta-analysis of the relationship between dietary tannin level and methane formation in ruminants from in vivo and in vitro experiments. *Journal of Animal Physiology and Animal Nutrition*, 96, 365-375.
- Jurgilevich A., Birge T., Kentala-Lehtonen J. et al. (2016). Transition towards Circular Economy in the Food System. *Sustainability*, 8(1), 69.
- Kesse-Guyot E., Fezeu L., Andreeva V. A. et al. (2012). Total and Specific Polyphenol Intakes in Midlife Are Associated with Cognitive Function Measured 13 Years Later. *J Nutr* 142 (1): 76–83.

- Kilic O. and Alkan I., (2006). The Developments in The World Hazelnut Production and Export. The Role of Turkey. *Journal of Applied Sciences*.6:1612-1616.
- King J.C., Blumberg J., Ingwersen L. et al. (2007). Tree Nuts and Peanuts as Components of a Healthy Diet. *The Journal of Nutrition - 2007 Nuts and Health Symposium*.
- Köksala A I., Artikb N., Şimşekc A. et al. (2006) Nutrient composition of hazelnut (*Corylus avellana L.*) varieties cultivated in Turkey, *Food Chem*;99: 509 – 515.
- Kornsteiner KM, Wagner KH, ElmadfaI. (2013). Phytosterol content and fatty acid pattern of ten different nut types. *Int J Vitam Nutr Res*; 83(5):263-70.
- Krikorian R., Erin L. Boespflug D. et al. (2012). Concord Grape Juice Supplementation and Neurocognitive Function in Human Aging. *Journal of Agricultural and Food Chemistry* 60 (23): 5736– 42.
- Kris-Etherton P.M., Hu F.B., Ros E. et al. (2007). The role of tree nuts and peanuts in the prevention of coronary heart disease: multiple potential mechanisms. *The Journal of Nutrition - 2007 Nuts and Health Symposium*.
- Lamport D. J., Deepa P., Moutsiana C. et al. (2015). The Effect of Flavanol-Rich Cocoa on Cerebral Perfusion in Healthy Older Adults during Conscious Resting State: A Placebo Controlled, Crossover, Acute Trial. *Psychopharmacology* 232 (17). Springer: 3227–34.
- Lamport D. J., Saunders C., Butler L. T. et al. (2014). Fruits, Vegetables, 100% Juices, and Cognitive Function. *Nutrition Reviews* 72 (12): 774–89.
- Lefèvre-Arbogast S., Gaudout D., Bensalem J. et al. (2018). Pattern of Polyphenol Intake and the Long-Term Risk of Dementia in Older Persons. *Neurology*. 2018 May 29;90(22):e1979-e1988.
- Letenneur L., Proust-Lima C., Le Gouge A. et al. (2007). Flavonoid Intake and Cognitive Decline over a 10-Year Period. *Am J Epidemiol* 165 (12): 1364–71.
- Lovins A., Braungart M., Stahel W. R., et al. (2014). *A New Dynamic: effective business in a circular economy*. Ellen MacArthur Foundation Publishing, 172.
- MacArthur, E. (2015). *Growth within: a circular economy vision for a competitive Europe*. Ellen MacArthur Foundation: Cowes, UK.
- MacArthur, E. (a) (2013). *Towards the circular economy: Economic and business rationale for an accelerated transition*. Ellen MacArthur Foundation: Cowes, UK.

- Macarthur, E. (b) (2013). Towards the circular economy: Opportunities for the consumer goods sector. Ellen MacArthur Foundation: Cowes, UK.
- Martineau AS., Leray V., Lepoudere A et al. (2016). A Mixed Grape and Blueberry Extract Is Safe for Dogs to Consume. *BMC Veterinary Research* 12 (1): 162.
- Mastroiacovo D., Kwik-uribe C., Grassi D. et al. (2015). “Cocoa Flavanol Consumption Improves Cognitive Function, Blood Pressure Control, and Metabolic Profile in Elderly Subjects: The Cocoa, Cognition, and Aging (CoCoA) Study - a Randomized Controlled Trial.” *The American Journal of Clinical Nutrition* 101: 538–48.
- Masullo M., Cerulli A., Mari A., et al. (2017). LC6MS profiling highlights hazelnut shells as a byproduct rich in antioxidant phenolics. *Food Research International*, 101, 180-187.
- Matson P. A., Parton, W. J., Power A. G., & Swift M. J. (1997). Agricultural intensification and ecosystem properties. *Science*, 277(5325), 504-509.
- McCleary B. V. (2003). Dietary fibre analysis. *Proceedings of the Nutrition Society*, 62, 3–9
- Mocchiari G., Bresciani L., Tsiountsioura M. et al. (2019) Dietary absorption profile, bioavailability of (poly)phenolic compounds, and acute modulation of vascular/endothelial function by hazelnut skin drink. *Journal of Functional Foods*, Volume 63, December, 103576.
- Moinard A. and Véronique Leray. (2018). An Administration of (poly)phenols Improves Endothelial Function and the Inflammatory Status in Dogs. In *Archives of Cardiovascular Diseases Supplements* 10(2):181.
- Monica Locatelli, Fabiano Travaglia, Jean Daniel Coïsson, et al. (2010) Total antioxidant activity of hazelnut skin (Nocciola Piemonte PGI): Impact of different roasting conditions. *Food Chemistry*, Volume 119, Issue 4, 1647-1655.
- Montella R., Coisson J. D., Travaglia F. et al. 2012. Bioactive compounds from hazelnut skin (*Corylus avellana* L.): Effects on *Lactobacillus plantarum* P17630 and *Lactobacillus crispatus* P17631. *Journal of functional foods*. 5:306-315
- Montella, R., Coisson, J. D., Travaglia, F., Locatelli, M., Malfa, P., Martelli, A., Arlorio, M. (2012). Bioactive compounds from hazelnut skin (*Corylus avellana* L.): Effects on *Lactobacillus plantarum* P17630 and *Lactobacillus crispatus* P17631. *Journal of functional foods*. 5:306-315.

- Moras B., Rey S., Vilarem G. et al. (2017). Pressurized water extraction of isoflavones by experimental design from soybean flour and Soybean Protein Isolate. *Food Chem*, 214, 9-15.
- Mrabti N. H., Jaradat N., Fichtali I. et al. (2018). Separation, Identification, and Antidiabetic Activity of Catechin Isolated from *Arbutus unedo* L. Plant Roots. *Plants*, 7(2).
- Murray A., Skene K., & Haynes K. (2017). The circular economy: An interdisciplinary exploration of the concept and application in a global context. *Journal of Business Ethics*, 140(3), 369-380.
- Niderkorn V., Gaudin E., Quereuil A. et al. (2018). Effects of dehydrated hazelnut pericarps and pellets of sainfoin as condensed tannins-containing resources on in vitro rumen fermentation. *International Symposium on the Nutrition of Herbivores*. Clermont-Ferrand, France. 2-6/09/2018.
- Odabaş H. İ., & Koca I. (2016). Application of response surface methodology for optimizing the recovery of phenolic compounds from hazelnut skin using different extraction methods. *Industrial Crops and Products*, 91, 114-124.
- Ogoh S. (2017). Relationship between Cognitive Function and Regulation of Cerebral Blood Flow. *Journal of Physiological Sciences* 67 (3). Springer Japan: 345–51.
- Osakabe N. & Terao J. (2018). Possible mechanisms of postprandial physiological alterations following flavan 3-ol ingestion. *Nutrition Reviews*, 76, 174-186.
- Ottaviani J. I., Kwik-Urbe C., Carl L. K. Et al. (2012). Intake of Dietary Procyanidins Does Not Contribute to the Pool of Circulating Flavanols in Humans. *American Journal of Clinical Nutrition* 95 (4): 851–58.
- Ottaviani JI, Heiss C, Spencer JPE. (2018) Recommending flavanols and procyanidins for cardiovascular health: Revisited. *Mol Aspects Med*. 2018 Jun;61:63-75.
- Ottaviani, J. I., Heiss, C., Spencer, J. P. E. (2018). Recommending flavanols and procyanidins for cardiovascular health: Revisited. *Molecular Aspects of Medicine*, 61, 63-75.
- Özdemir K. S., Yılmaz C., Durmaz G. (2014). Hazelnut skin powder: A new brown colored functional ingredient. *Food Research International* 65 291–297.
- Özdemir K.S., Yılmaz C., Durmaz G. et al. (2014). Hazelnut skin powder: A new brown colored functional ingredient. *Food Research*, 65, 291-297.

- Papargyropoulou E., Lozano R., Steinberger J. K. et al. (2014). The food waste hierarchy as a framework for the management of food surplus and food waste. *Journal of Cleaner Production*, 76, 106-115.
- Parajó et al. (2004). *Trends in Food Science & Technology* 15:115–120
- Patra AK., SAxena J. (2011). Exploitation of dietary tannins to improve rumen metabolism and ruminant nutrition. *Journal of the Science of Food and Agriculture*, 91, 24-37.
- Pearc, D. W., & Turner R. K. (1990). *Economics of natural resources and the environment*. JHU Press.
- Pérez J, Muñoz-Dorado J, de la Rubia T. et al. (2002). Biodegradation and biological treatments of cellulose, hemicellulose and lignin: an overview. *Int Microbiol.* 2002 Jun; 5(2):53-63.
- Pérez-Jiménez J., Neveu V., Vos F. et al. (2010). Identification of the 100 richest dietary sources of (poly)phenols: an application of the Phenol-Explorer database. *Eur J Clin Nutr.* 2010 Nov; 64 Suppl 3:S112-20.
- Pérez-Jiménez J., Neveu V., Vos F. et al. (2010). Identification of the 100 richest dietary sources of (poly)phenols: an application of the Phenol-Explorer database. *Eur J Clin Nutr.* 2010 Nov; 64 Suppl 3:S112-20.
- Prakash K, Dinu S. Chandran R. K et al. (2016). Correlations between Endothelial Function in the Systemic and Cerebral Circulation and Insulin Resistance in Type 2 Diabetes Mellitus. *Diabetes and Vascular Disease Research* 13 (1): 49–55.
- Quijada J., Drake C., Gaudin E. et al. (2018). Condensed Tannin changes along the digestive tract in lamb fed sainfoin pellets or hazelnut skins. *Journal of Agricultural and Food Chemistry.* 66, 2136-2142.
- Robbins R. J., Leonczak J., Johnson J. C. et al. (2009). Method performance and multi-laboratory assessment of a normal phase high-pressure liquid chromatography-fluorescence detection method for the quantitation of flavanols and procyanidins in cocoa and chocolate containing samples. *J Chromatogr A*, 1216(24), 4831-4840.
- Rodriguez-Mateos A., Vauzour D., Krueger C. G. et al. (2014). Bioavailability, bioactivity and impact on health of dietary flavonoids and related compounds: an update. *Arch Toxicol*, 88, 1803-53.

- Sahathevan R., Brodtmann A., and Donnan G. (2012). Dementia, Stroke, and Vascular Risk Factors; a Review. *International Journal of Stroke* 7 (1): 61–73.
- Sánchez C. (2009). Lignocellulosic residues: Biodegradation and bioconversion by fungi. *Biotechnology Advances* Volume 27, Issue 2, March–April, Pages 185-194.
- Santamaría B., Salazar G., Beltrán S., & Cabezas J. L. (2002). Membrane sequences for fractionation of polyphenolic extracts from defatted milled grape seeds. *Desalination*, 148(1), 103-109.
- Scalbert A, Williamson G. (2000). Dietary intake and bioavailability of polyphenols. *J Nutr.* Aug; 130(8S Suppl):2073S-85S.
- Schmitzer, V., Slatnar, A., Veberic, R. et al. (2011), Roasting Affects Phenolic Composition and Antioxidative Activity of Hazelnuts (*Corylus avellana* L.). *Journal of Food Science*, 76: S14-S19.
- Scholey A.B., French S.J., Morris P. J., et al. (2010). Consumption of Cocoa Flavanols Results in Acute Improvements in Mood and Cognitive Performance during Sustained Mental Effort. *Journal of Psychopharmacology* 24 (10): 1505–14.
- Schroeter H., Heiss C., Balzer J. et al. (2006). -Epicatechin Mediates Beneficial Effects of Flavanol- Rich Cocoa on Vascular Function in Humans. *Proceedings of the National Academy of Sciences* 103 (4): 1024–29.
- Schroeter H., Heiss C., Spencer J. P. E. et al. (2010). Recommending flavanols and procyanidins for cardiovascular health: Current knowledge and future needs. *Molecular Aspects of Medicine*, 31, 546-557
- Serra A., Maci A., Romero M-P et al. (2013). Distribution of procyanidins and their metabolites in rat plasma and tissues in relation to ingestion of procyanidin-enriched or procyanidin-rich cocoa creams. *Eur J Nutr.* Apr;52(3):1029-38
- Shahidi F., Alasalvar C, Liyana-Pathirana CM. (2007). Antioxidant phytochemicals in hazelnut kernel (*Corylus avellana* L.) and hazelnut byproducts. *J Agric Food Chem.* Feb 21;55(4):1212-20. Epub 2007 Jan 24.
- Shahidi F., Alasalvar C., Liyana-Pathirana C.M. (2007). Antioxidant phytochemicals in hazelnut kernel and hazelnut byproducts. *Journal Agricultural and Food Chemistry*, 55, 1212-1220.

- Shrotri A., Tanksale A., Beltramini JN. Et al. (2017). Chapter Two - Catalytic Conversion of Structural Carbohydrates and Lignin to Chemicals. *Advances in Catalysis*, Volume 60, 2017, Pages 59-123
- Soliman G. A. (2019). Dietary Fiber, Atherosclerosis, and Cardiovascular Disease. *Nutrients*, 11(5), 1155.
- Stahel W. R. (2016). Circular economy: a new relationship with our goods and materials would save resources and energy and create local jobs. *Nature*, 531(7595), 435-439.
- Stevenson L., Phillips F., O'Sullivan K. et al. (2012). Wheat bran: its composition and benefits to health, a European perspective. *International Journal of Food Sciences and Nutrition*; 63(8): 1001–1013
- Stuart T. (2009). *Waste: Uncovering the Global Food Scandal*; Penguin Books Limited: London, UK.
- Surek E., Buyukkileci A.O. (2017). Production of xylooligosaccharides by autohydrolysis of hazelnut (*Corylus avellana* L.) shell. *Carbohydr Polym.* 2017 Oct 15;174:565-571.
- Tan S. Y., Dhillon J., and Richard D Mattes R. D. (2014) A review of the effects of nuts on appetite, food intake, metabolism, and body weight1–3. *Am J Clin Nutr*;100(suppl):412S–22S.
- Tapsel LC. (2014). Foods and food components in the Mediterranean diet: supporting overall effects *BMC Med.* Jun 16;12:100.
- Tokuşoğlu O. and Hall C. (2011). Introduction to bioactives fruits and cereals. In: *Fruit and Cereals Bioactives* (eds Tokuşoğlu O. and Hall C.), pp.3-8. CRC Press.
- Torabian S., Haddad E., Rajaram S. et al. (2009). Acute effect of nut consumption on plasma total (poly)phenols, antioxidant capacity and lipid peroxidation. *J Hum Nutr Diet.* 2009 Feb;22(1):64-71.
- Tucker M.P., Kim K.H., Newman M.M. (2003). Effects of Temperature and Moisture on Dilute-Acid Steam Explosion Pretreatment of Corn Stover and Cellulase Enzyme Digestibility. *Applied Biochemistry and Biotechnology*. Volumes 105, Number 1 - 3, ISSN: 0273–2289
- Vaisman, Nachum V. and Eva Niv. (2015). Daily Consumption of Red Grape Cell Powder in a Dietary Dose Improves Cardiovascular Parameters: A Double Blind, Placebo-

Controlled, Randomized Study. *International Journal of Food Sciences and Nutrition* 66 (3): 342–49.

- Xu Y. X., M.A.Hanna M. A. (2009). Synthesis and characterization of hazelnut oil-based biodiesel. *Industrial Crops and Products* Volume 29, Issues 2–3, March, Pages 473-479
- Zamora-Ros R, Knaze V, Rothwell JA. (2016) Dietary polyphenol intake in Europe: the European Prospective Investigation into Cancer and Nutrition (EPIC) study. *Eur J Nutr.* Jun;55(4):1359-75.
- Zarbin PHG, Yonashiro M, Perissini J., Waldir (1998). An Alternative Route for the Synthesis of (E)-(+)-5(S)-Methylhept-2-en-4-one (Filbertone). *Journal of the Brazilian Chemical Society*; 9 (6): 583.
- Zinnanti C., Schimmenti E., Borsellino V. (2019). Economic performance and risk of farming systems specialized in perennial crops: An analysis of Italian hazelnut production. *Agricultural systems* v.176 pp. 102645.

Websites

- Camera di Commercio Cuneo, detection time October 2019
<http://www.cuneoprezzi.it/ingrosso/ALIMENTARI/index?category=35> (accessed 25/10/2019)
- FAOstat (UN Food and Agriculture Organization, Statistics Division). Hazelnuts (with shell); Crops by Region, World List, Production Quantity, 2017.
<http://www.fao.org/faostat/en/#data/QC>. (accessed 07/31/2019)
- GİRESUN COMMODITY EXCHANGE STATISTICAL DATA
<http://www.giresunb.org.tr/EN/statistic.php> (accessed 10/29/2019)
- Government of the Netherlands - From a linear to a circular economy.
<https://www.government.nl/topics/circular-economy/from-a-linear-to-a-circular-economy> (accessed 10/25/2019)
- Ministero della salute (2009). Altri nutrienti e altre sostanze ad effetto nutritivo o fisiologico.
http://www.salute.gov.it/portale/temi/p2_6.jsp?lingua=italiano&id=1423&area=Alimenti%20particolari%20e%20integratori&menu=integratori (accessed 10/23/2019)
- Mintel's GNPD database Global New Product Database.
<https://www.mintel.com/global-new-products-database> (accessed 08/19/2019)
- Open-BIO. (2015) Opening bio-based markets via standards, labelling and procurement.
<https://www.biobasedeconomy.eu/app/uploads/sites/2/2017/07/Acceptance-factors-for-bio-based-products-and-related-information-systems.pdf> (accessed 09/09/2019)
- PBL, Netherlands Environmental Assessment Agency (2017). Food for a circular economy.
<https://www.pbl.nl/en/publications/food-for-a-circular-economy> (accessed 08/19/2019)
- Persistence market research. (2018). Global Market Study on Hazelnut: Increasing Demand to be Observed in the Pharmaceuticals Sector During 2018 – 2026.
<https://www.persistencemarketresearch.com/market-research/hazelnut-market.asp> (accessed 07/26/2019)
- Peter Lacy, Jakob Rutqvist. Waste to Wealth, Springer Nature (2015).
<https://thecirculars.org/content/resources/Accenture-Waste-Wealth-ExecSumFINAL.pdf> (accessed 08/19/2019)

- Transparency market research. (2013). (poly)phenols Market by Product (Grape seed, Green tea, Apple and Others), by Application (Functional beverages, Functional food, Dietary supplements and Others) - Global Industry Analysis, Size, Share, Growth, Trends and Forecast, 2012 – 2018.
<http://www.transparencymarketresearch.com/polyphenol-market.html> (accessed 07/26/2019)
- TRANSPARENCY MARKET RESEARCH. (2017). (Poly)phenols Market by Product (Grape seed, Green tea, Apple and Others), by Application (Functional beverages, Functional food, Dietary supplements and Others) - Global Industry Analysis, Size, Share, Growth, Trends and Forecast, 2012- 2018.
<https://www.transparencymarketresearch.com/polyphenol-market.html> (accessed 8/19/2019)
- USDA National Nutrient Database for Standard Reference. (2018). Hazelnut composition.
<http://ndb.nal.usda.gov/ndb/foods/list> (accessed 07/26/2019)
- Ward, S.M., Holden, N.M., White, E.P., Oldfield, T.L. (2016). The 'circular economy' applied to the agriculture (livestock production) sector.
http://ec.europa.eu/information_society/newsroom/image/document/201648/ward_circular_economy_applied_to_the_livestock_production_sector_brussels_2_40231.pdf (accessed 08/19/2019)
- WHO (2011) Global Status Report on Noncommunicable Diseases 2010. Geneva: World Health Organisation.
https://www.who.int/nmh/publications/ncd_report_full_en.pdf (accessed 08/19/2019)
- WHO. (2005) Ecosystems and Human Well-Being: Health Synthesis. A Report of the Millennium Ecosystem Assessment. Geneva: World Health Organization
<https://www.millenniumassessment.org/documents/document.356.aspx.pdf> (accessed 08/19/2019)