INTELLECTUAL OUTPUT O1

Economic and Health Benefits, Social Opportunities and Health Claim as a tool for marketing extra virgin olive oil

Date: 11th March 2020

ARISTOIL CAPITALIZATION

ΙΔΡΥΜΑ ΚΡΑΤΙΚΩΝ ΥΠΟΤΡΟΦΙΩΝ IKY

Erasmus+

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2 Intellectual Output Description

A study and collection of case studies of the use of health claims and the results that can bring on the local competitiveness and the environmental benefits. The use of health claims can bring health and economic benefit in multiple ways. i.e environmentally, employability. The quantification of this benefit and the collection of case studies can give a proof of concept. This documentation is needed for the persuasion of the stakeholders for its usefulness. The potential economic benefit should be measured through a scientific methodology. The collection of the case studies, the best practices and the methodology for measuring it or presenting the potential benefit will be published in a book and the whole context will be available through the project website.

Part of this Intellectual Output was sent for publication to one of the most known magazines for Agriculture and Food and it will be published as a part of dissemination activity of the project. Copy of the article will be available after publication to the National Agency as proof.

Languages: English, Greek, Italian, Turkish
Media: Publication: The Output will be presented as a “Book”
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Contents

4 Methodology

The Output type is Study / analysis – Data collection / analysis. Data will be collected for each participating country from official sources and recent cases will be presented.
Copartners will contribute equally to the output.

Official links to competent authorities and European Commission presenting data, which are updated regularly are useful to include them. Output will be "self-updated" and official data only should be used, from official resources. A lot of official information could be found also in EU Publications. In case written permission required for data acquisition, please consider to obtain it. Do not use data without permission and do not obtain data unofficially. Always make an appropriate reference to the source of your information, even if it is not official.

For administrative and technical purposes try to collect the information referring to the contents previously described. In case there are additional information, inform the Beneficiary and the Leading Organisation for this Output before preparing the material. It is important all partners to have the same format.

This output will provide the basis for the justification of the frame of Short-term joint staff training events. It will fully exploit the Intellectual Outputs of Interreg ARISTOIL project and will exploit the principles of ISO 29990:2010 for nonformal education and training. In this output the partnership will include the quality control manual of this event. It is not a requirement from the approved content of the application or the National Agency but it was considered that it will be useful for future products from this partnership or other applicants and also as an evaluation tool for the national Agency for this kind of events.

5 Introduction

Food labeling is becoming increasingly complex from a legal point of view as it incorporates a great deal of information. It is no exaggeration to say that labeling has become so complex that it is very easy to mislead consumers.

As food production is becoming more and more sophisticated and more and more ingredients are available in the industry, extended information is therefore required to appear on a label of a finite size. The effect for processors is to make it more and more difficult to balance the design and dimensions of a label with the requirements of the legislation.
The label must also satisfy the consumer's need or interest in a healthy diet, as well as their interest in ingredients and their origin. Nutritional values should also be placed in a small place, such as a label.

The information described above is important and must be displayed on the label and used for the presentation, marketing and advertising of products in a clear, accurate and meaningful manner for the consumer.

Food information should not attribute to any foodstuff the properties of preventing, treating or curing any human disease, nor referring to such properties (except natural mineral waters and special nutritional foods). These principles apply to their advertising and presentation of foodstuffs, shapes, forms, packaging materials, etc.

The European Union has laid down detailed rules for labeling. However, information on nutrition and health claims has its own legal framework. Of course, in this case, the basic provision is that the allegations must not mislead the consumer. However, in many cases in different Member States in the past it has been found that these provisions could be open to different interpretations.

The food industry has responded to the increased demand from consumers for information presented on a food label, providing this information to various foods. The evolution of food science and technology has resulted in the production of more and more ingredients, resulting in a greater workload for food scientists in the industry. Evolution could be considered positive for providing relevant information to the consumer, in any case for the food industry, it is also an opportunity to use the claims as a marketing tool.

6 Terms

- 'food information': information on a foodstuff and made available to the final consumer by labeling, other accompanying material or any other means, including modern technology tools or oral communications
- 'mandatory food information': the information required to be provided to the final consumer in accordance with the relevant provisions
- 'label' means any mark, trademark, trade mark, image or other description which is written, printed, perforated, marked, embossed or imprinted or attached to the food packaging or container.
- 'labeling' means any indications, marks, trademarks, trade names, images or symbols referring to a foodstuff and placed on any packaging, document, plate, label, ring or collar accompanying or referring to that foodstuff.
- 'field of vision': all surfaces of a package that can be read from an angle
- 'main field of vision': the field of view of the packaging that the consumer is most likely to see at first glance at the time of purchase
- 'readability': the appearance of information on the packaging, through which the information is visually accessible to the general public and determined by a variety of elements
- 'field of vision': all surfaces of a package that can be read from an angle
- 'main field of vision': the field of view of the packaging that the consumer is most likely to see at first glance at the time of purchase
- 'primary ingredient' means the food ingredient (s) accounting for more than 50% of that food
- "date of minimum shelf life of a food": the date by which the food retains its particular properties in suitable storage conditions

7 Specifications

European food law is extensive and detailed in formulating its requirements. Easily accessible to anyone interested in the website of the European Food Safety Authority (EFSA) and other competent national services and organizations.

The prospective exporter must be aware of the legal and regulatory requirements and provide the necessary resources for their consistent implementation. The employment of competent scientific staff guarantees the exporter's commitment to comply with food safety systems, to properly label and recommend products.

Nutrition Declaration

A key element of the labeling is the nutrition declaration, usually in the form of a table with information on energy value, quantities of fat, protein, carbohydrates and salt. The nutritional statement may be supplemented by indicating the amounts of one or more monounsaturated, polyunsaturated fats, analysis of carbohydrates in sugars, polyols, starch, edible fibers and vitamins or minerals. 100 ml or 100% expressed in the analysis of the food by the manufacturer or even in a calculation based on the known or actual average values of the ingredients used. Value shall also be expressed per unit or per unit of consumption provided that the portion or unit used is quantified and the number of units or units contained in the package is stated.

The **nutrition declaration** may be supplemented by indicating one or more of the following:

1. Monounsaturated
2. Polyunsaturated
3. Polyols
4. Starch
5. Edible fibers
6. Vitamins or minerals
7. Edible fibers
8. Energy value or energy value together with the quantities of fat, saturated, sugars and salt

Energy Value Calculation

Value are based on:

- Analysis of the food by the manufacturer
- Calculated on the basis of the known or actual average values of the ingredients used, or
- Calculation based on generally defined and accepted data

How do they express themselves?

- Expression per 100 g or per 100 ml
- Expression on a per-serving or per-unit basis provided that the portion or unit used is quantified on the label and that the number of portions or units in the package is stated in addition to the expression form per 100 g or per 100 ml
- When the amounts of nutrients are expressed on a per-serving or per-unit basis only, the energy value is expressed per 100 g or per 100 ml and on a per-unit or per-unit basis only.

- The portion or unit used is very close to the nutrition statement

Highlights

In general, the following information must be given on the packaging:

- Ingredients (quantities in% per case and in descending order)
- Tips for allergies
- Consumption before date
- Net weight and "e" symbol
- Producer information (EU address)
- Origin of the product
- Lot code (traceability)
- Bar code reflecting GTIN (Global Item Number) https://www.gtin.info/
- Instructions for preparation, use and storage

In some countries like Germany some features of the packaging are important in the market. The "readability" of the information on the packaging, the size and intensity of the indications, the "field of vision", the surfaces of the packaging that can be read from an angle and the "main field of vision" the field of vision of the packaging which is most likely to be seen by the consumer at the time of purchase.

Traceability

Traceability consists of the ability to trace the origin of products across the food chain, from farm to processing, transport, storage, distribution and retail to the consumer.

Food business operators must be able to identify the origin of ingredients incorporated in food, suppliers and customers. Business operators shall establish systems and procedures that make this information available to the competent authorities upon request.

Foodstuffs must bear an appropriate label or identification mark to facilitate their traceability and the withdrawal of dangerous foods from the market.

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- The portion or unit used is very close to the nutrition statement

Highlights

Vision of the packaging which is most likely to be seen by the consumer at the time of purchase.

Sugars

1. Sugar-free - The claim that a food does not contain sugar, and any claim that may make the same sense to the consumer, can only be used where the product contains no more than 0.5g of sugar per 100 g or 100 ml.
2. without added sugars - The assertion that a food does not contain added sugars, and any claim that may have the same meaning to the consumer, may be used only when the product contains no additional monosaccharides or disaccharides or other food used for its sweetening properties. If there are natural sugars in the food, the label shall also bear the following indication "Contains Natural Sugars".
3. low sugar content - The claim that a food is low in sugar, and any claim that may make the same sense to the consumer, may be used only when the product contains no more than 5 g of sugar per 100 g for solid foods or 2.5 g of sugar per 100 ml for liquid foods.

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Nutrition Health Claims

Health Claim: Any claim that states, implies or leads to the conclusion that there is a relationship between a food category, a food or its ingredient and health.

Allegedly reduced risk of disease: Any health claim that indicates, implies or leads to the conclusion that consumption of a food category, food or ingredient significantly reduces the risk factor for the occurrence of a human disease.
health that indicates, implies or leads to the conclusion that consumption of a food category, food or ingredient significantly reduces the risk factor for the occurrence of a human disease.

Only if the following information is included:

- Statement highlighting the importance of a varied and balanced diet and a healthy lifestyle
- The quantity of food and the way of consumption needed to achieve the beneficial effect stated in the claim
- Declaration to people who should avoid eating and
- Appropriate warning for products that may be a health hazard if consumed excessively

When not allowed!

- When they imply that non-consumption of food may affect health
- When referring to the rate or amount of weight loss
- When referring to recommendations from individual physicians or health professionals and other associations
- Health claims other than those mentioned to reduce the risk of developing a disease, such as e.g. the role of a nutrient or other substance in the growth, development and functioning of the body can be used when based on generally accepted scientific data and are easily understood by the average consumer.

What Not to Use Claims?

- Be false, ambiguous or misleading
- Doubts about the safety and / or nutritional value of other foods
- Encourage or show acceptable consumption of an excessive food
- Indicate, imply or imply that a balanced and varied diet may not provide sufficient quantities of nutrients in general
- To refer to changes in the functions of the organization, which could cause feelings of fear in the consumer or exploit his fear, either through verbal or visual, graphic or symbolic representations.

When are they allowed?

- Where the presence, absence or reduced content of a claimed nutrient or other substance in a foodstuff or foodstuff has a proven beneficial nutritional or physiological effect, according to generally accepted scientific data
- Where the claimed nutrient is contained in the finished product in a significant quantity as defined in Community legislation or, where such rules are not available, in a quantity which will produce the nutritional or physiological effect stated in the claim in accordance with

generally accepted scientific evidence data, or not contained or contained in a reduced amount, giving rise to the nutritional or physiological effect of the claim in accordance with generally accepted scientific data

- The nutrient or other substance claimed is in a form that can be used by the body!
- The quantity of product expected to be consumed provides a significant amount of the claimed nutrient as defined in the legislation or, where such rules do not exist, a significant amount that will bring about the nutritional or physiological effect stated in the claim. generally accepted scientific data
- Use of nutrition and health claims is only permitted if the average consumer is expected to understand the beneficial effects as stated in the claim.
- Nutrition and health claims refer to ready-to-eat foods according to the manufacturer's instructions
- Nutrition and health claims are based on and substantiated by generally accepted scientific data
- The food business operator using a nutrition or health claim justifies the use of that claim
- Competent authorities may require the food business operator or person placing a product on the market to provide all relevant data and data demonstrating compliance with applicable law.

Comparison between foods

Only foodstuffs of the same category can be compared, taking into account a range of foods in that category.

The difference in the amount of a nutrient and / or energy value must be reported, and the comparison should concern the same amount of food.

The comparative nutrition claims compare the composition of the food in question with a series of foods which do not allow them to be claimed, including foods of other trade names.

Olive Oil Health Claims

Procedure EU Register on nutrition and health claims
The information below is derived from:
ec.europa.eu/food/safety/labelling_nutrition/claims/health_claims_en

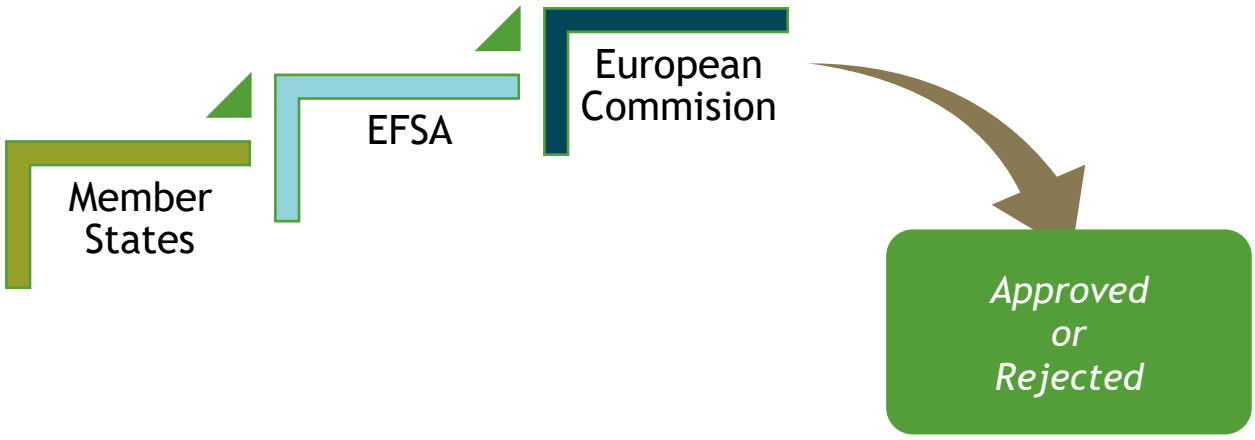
Please check the above link for relevant updates or scan the QR code from your smartphone

The authorisation procedure involves:

1. The applicant
2. The competent national authorities
3. European Food Safety Authority (EFSA)
4. The European Commission

It is a three (3) step procedure

1. Applicants must submit an application to an EU-country's competent authority that checks admissibility before transmitting it to EFSA. The Commission's implementing rules, established by Commission Regulation (EC) No 353/2008, inform applicants what their application should include. More guidance on the definition and classification of the scientific data for the assessment of a health claim is available on the EFSA website. EFSA informs the national competent authorities and the Commission of the receipt of the application and gives a publicly available opinion The Commission prepares a draft decision and submits it to the Standing Committee on Plants, Animals, Food and Feed after EFSA publishes its opinion.
2. After a favourable opinion of the Standing Committee on the Food Chain and Animal Health, the European Parliament and the Council have the right of scrutiny on the Commission's draft decision
3. If there is no objection, the Commission adopts the draft decision.



More specifically for Olive Oil Polyphenols there is a specific provision in Commission Regulation (EU) No 432/2012 (data.europa.eu/eli/reg/2012/432/oj), where the claim may be used only for olive oil which contains at least 5 mg of hydroxytyrosol and its derivatives (e.g. oleuropein complex and tyrosol) per 20 ml of olive oil. In order to bear the claim information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 20 ml of olive oil.

The following table is part of the Annex LIST "OF PERMITTED HEALTH CLAIMS" of the Regulation.

Nutrient, substance, food or food category	Claim	Conditions of use of the claim	Conditions and/or restrictions of use of the food and/or additional statement or warning	EFSA Journal number	Relevant entry number in the Consolidated List submitted to EFSA for its assessment
Olive oil polyphenols	Olive oil polyphenols contribute to the protection of blood lipids from oxidative stress	The claim may be used only for olive oil which contains at least 5 mg of hydroxytyrosol and its derivatives (e.g. oleuropein complex and tyrosol) per 20 g of olive oil. In order to bear the claim information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 20 g of olive oil.		2011;9(4):2033	1333, 1638, 1639, 1696, 2865

'Health claim' refers to any claim that indicates, implies or leads to the conclusion that there is a relationship between a food category, food or ingredient and health. Only if the following information is included:

- Statement highlighting the importance of a varied and balanced diet and a healthy lifestyle
- The quantity of food and the way of consumption needed to achieve the beneficial effect stated in the claim

Declaration to persons who should avoid eating and

- Appropriate warning for products that may pose a health risk if consumed excessively
- When are they not allowed?
- When they imply that non-consumption of food may affect health
- When referring to the rate or amount of weight loss
- When referring to recommendations from individual physicians or health professionals and other associations

Therefor health claims other than those mentioned to reduce the risk of developing an illness, such as e.g. the role of a nutrient or other substance in the growth, development and functioning of the

body can be used when based on generally accepted scientific data and are easily understood by the average consumer.

The background to health claims is based on the logic described in Codex Alimentarius, health claims are any presentation that states, indicates or implies that there is a relationship between a food or an ingredient of that food and health. In particular it further defines three categories of health claims that include:

Nutrition claims for dietary functions: "Nutrition claim that describes the physiological role of the nutrient in growth, development and normal body functions".

- other operating claims:
    1. "These claims relate to specific beneficial effects of the consumption of foods or their constituents in the context of total nutrition in the normal functions or biological activities of the body. or maintaining health.
    2. Allegations concerning the limitation of the risks of disease: 'Allegations about the consumption of a food or food ingredient in the context of an overall diet with a reduced risk of developing a disease or health-related condition'

How the food industry perceives Health Claims

Recognizing that it is a serious consumer outreach tool, the food industry is constantly seeking new data to achieve this goal. The question is always whether there is a real need to invoke a health claim. With the current legislative framework, it has largely ceased to have a constant confusion about what can and should not be mentioned on a food label. In fact, what happens in many cases is that a myth is created around the claim, making the myth itself more important than the claim.

Under no circumstances is a single claim sufficient to guarantee high sales for a product and in no case should the industry focus more on the claim than on the consumer itself. In such cases the innovation of the product is lost.

From the consumer side, according to surveys, they appear to be particularly skeptical to suspicious. Consumer criteria are: how much I like a product, the company that makes it and only if they can't decide will pay attention to the label.

15 Social and Economic Development and Impact measurement

The olive sector has a significant social, economic as well as environmental role in the Mediterranean countries. Olive oil is main product of this sector and it has a major role on economic development and public health nutrition. In general, establishing linkages between nutrition and healthy life/disease prevention could cause social and economic development of countries. Repeated educational exposure of olive oil health claims does not only create an awareness about olive oil consumption of consumers but also results in increased consumption of healthy nutrition diet. In addition to its social, environmental, and cultural value, olive oil has a vital importance especially for olive growing cities due to its potential to enhance the economy and generate employment. Production "extra virgin olive oil (EVOO) with health claim" at a sustainable price will make olive oil available for everybody. These will improve rural employment as well as healthy nutrition/disease prevention of public.

Production of high value added products like EVOOs with health claims have social and economic effects such as increases in rural development, increases in income of farmer/producer and decreases in government/personal expenditures which caused by diseases (cancer, cardiovascular diseases etc.), training of consumers to create awareness of the healthy olive oil, preserved olive tree, biodiversity, ecology, history, culture of the area and heritage of culinary, maintenance of local jobs, promotion of family enterprises, traditional skills and food traditions.

Back in 1985, most health claims on food, were related to their sensory aspects, and only 10.4% of were related to nutrition and health. Today is more than 65% (2009 data) according to Kim et al., 2009. **V.J. van Buul and F. Brouns** have made a deep analysis of the use of Health claims as Marketing Tools. In fact, their conclusions in 2009 are used extensively today for the promotion and placing new products in the market at world level.

Several parameters affecting consumers' choice, such as:

- Food category for example is an important independent variable affecting the dependent consumer attitude toward a Health Claim (HC)
- The brand name of the product, not all brands have the same acceptance from the consumer and the same degree of confidentiality
- Nutritional information on product labels can influence the consumer evaluation of the product
- Presenting information about health can influence the need for a product
- Acceptance of the proposed ingredient by the consumer

From the above is obvious that both the type of product and the brand are of most importance to the acceptance of an ingredient and its link with the HC. Food products accompanied with a HC fall into a food product category. This means that these products have to face the difficulties for the acceptance as products plus the difficulties faced from suspicious consumer.

To return back to the product category criterium the authors emphasize the principle which considers non healthy food as testier!!! Thus, a tasty food product carrying a HC has to face this obstacle as well. In our case olive oil has its own characteristics for each separate area in the involved countries, which are a kind of a tradition and story or background. Thus, this obstacle is not an issue for this product. HC came recently and most of its effects were known but not proven until today scientifically. Olive Oil in some cases is sold as "pharmaceutical" product. In this case taste is not important, as pharmaceutical industry never paid much attention to this issue. However, considering that olive oil is food product it is appropriate to neglect the parameter of taste.

The location of the food product is also a major factor according to the above-mentioned authors. It is important for the consumer the location of the product sold. A product accompanied with a HC cannot be sold in a small market usually, especially in countries like Greece, where consumer thinks that only medium quality products are sold in these places. However, after the 2010 economic crisis most of these small sized shops focused on quality products including functional foods.

Behind a HC there is a strong scientific background as already mentioned. Consumers should be given a simplified version of this background in order to understand which ingredients and foods confer what kind of specific health benefits. According to Daniel et al., (2009) most consumers only understand health related messages if the right things are communicated to the right people on the right product. In order for the consumer to understand the concept of HC there should be a balance between substantiation and understandability. By balance we mean that labeling should not be misleading, be well-substantiated and the claim should be understandable. As it can be understood it is not an easy task for the food industry.

According to Mariotti et al. (2010) there are six things confuse the consumer:

1. Lexical issue as average consumer may find it difficult to understand the scientific terms that the food regulatory authorities' prescription of HC
2. HCs could go beyond scientific truth
3. Consumers confuse between food and diet in a way that they tend to think that one product with a HC could balance out another unhealthier product
4. That the more they take of a product, the stronger the effect will be
5. Some consumers might think that a mere healthy diet is enough to prevent diseases such as cardiovascular disease, diabetes type 2 and cancer (this is our case with olive oil)
6. Food processors should direct the right HCs to the right consumer groups to ensure an adequate effect

Regarding the impact on local society, the answer to this question is in fact hypothetical as the Interreg ARISTOIL results were not actually implemented. It was not a simple task to establish a cluster as it was expected at least in Greece, due to the fact that the terms for funding were not actually designed for a cluster but for a profit company, which is not the case of this study, as part of ARISTOILCAP project.

However, the team of this project is expecting through training seasons, even though distance learning as this training material is designed to provide the knowledge initially and to establish the base for farmers and olive oil mills with the concept of HC.

Thus, ARISTOILCAP will accomplish what the Interreg project did not manage. The same time the consortium will continue the effort for raising funding for the cluster initiation and development of the relevant standards.

Success will be measured according to farmers and mills participation and training completion. These will be our main indices. The next chapter is describing the cluster concept and structure which is still under development. The initial feedback for the local society seems to be encouraging as it will give an added value to a product with strong competition and the same time there will be an exchange of information among participating countries regarding the use of HC and the scientific background behind it and how this could be communicated to the farmers.

As a case study it will be an example on how to increase the added value of a product transform it to a functional food (FF) and increase local communities income.

18

Cluster Initiation

General Information

A cluster is under development under the name “MED HEALTH OLIVE OIL CLUSTER “ARISTOIL”. The proposal took place under the frame of the Interreg project ARISTOIL. The idea was that Olive mils and olive oil producers could be organized under a certain statute, trained according to the outputs of ARISTOIL and ARISTOIL CAP projects, follow the quality control requirements as defined in ARISTOIL and dispose their product through the channels of the cluster. The partnership will also present considering as well the described case studies, how a health claim could turn in favor of the producers the economic environment.

Definition of the functioning frame of the cluster is under development, thus the partnership will present the cluster as a real case study and unique as an entity. For this purpose, the partnership asked the National Agency to deliver the final version of the Output later this year. It will be for the benefit of the project and Erasmus+ KA2 VET in general to present a case which has not taken place before in any other country.

Definition

Cluster is the partnership of financial entities engaged in a common product or service. Cluster usually involves economic entities that have an indirect economic benefit from the creation and development of the Cluster.

Key players

Major key players are the following economic entities that contribute to the production of Health Claim Olive Oil.

- Olive growers
- Oil mills
- Standardizers
- Logistics - Points of sale
- Laboratories for measuring phenolic, organoleptic, chemical, etc. characteristics

Scope

There three basic scopes for the cluster establishment, (a) to improve the quality of the product through innovative and scientifically based extraction techniques, (b) to give added value to the product and consequently increase farmers’ income and (c) production of a “biofunctional food”.
The most important is to disseminate the value of the high concentration of polyphenols olive oil and the scientific fact that not all olive oils are the same. This will differentiate the product and the production zone.

Scientific Base

According to Regulation (EC) 432/2012 it is stated clearly that Polyphenols in olive oil help protect blood lipids from oxidative stress. The claim can only be used for olive oil which contains at least 5 mg of hydroxytyrosol and its derivatives (e.g. oleuropein and tyrosol complex) per 20 g of olive oil.

A successful story

The success of a cluster is to ensure the quality of the product. Those who participate:

- must meet the basic principles of harvesting, processing and disposal of HC Olive Oil,
- receive checks and certifications as described in the Cluster operating protocol.

The olive oil that will be marketed with the designation H.C. ARISTOIL, will have:

1. D3> 500mg / Kg
2. will not have negative organoleptic characteristics
3. will be free of pesticides and other harmful elements

To these bodies, a special logo of recognition of participation in the Med Health Olive Oil Cluster "ARISTOIL" and a corresponding mark on the certified products are available. A special certification system will be developed for each category of body. The final product will be tested, in several stages, with methods developed in the "Aristoil" project. Producers and Oil Mill workers will be trained according to the "AristoilCAP" standards training program.

Producers

The certification control of the producers is done in the field and it is related to the cultivation methods applied and mainly the harvesting and the extraction process in certified olive mills. The certification process is similar to that of the Organic Farming. It is necessary to check the final product in respectively certified laboratories. Non-compliance can lead to the lifting of certification.

Olive mills

The oil mill must have basic specifications corresponding to the PDO certification (temperature sensors, fruit residence sheds, etc.) process and comply with the production standards of Health Claim olive oil (fruit residence time, massage temperature 27 ^{0}C, extraction time 30 min, avoid water etc.) The management body of the cluster undertakes the promotion of the certified Cluster ARISTOIL olive mills, in order to inform the oil producers.

Processors

The standard must meet the specifications of PDO and BIO (organic). The tanks must be double-walled for a constant temperature, be connected to an inert gas source, have an electronic system for recording the conditions of residence of olive oil in the premises.
The premises olive oil should be checked in each batch of standardization and ensure that the standard products are transported.

Indicate on the packaging the limit of the phenolic concentration, together with the date of issue of the certificate.

Logistics - Points of Sale

Certified logistics have the right to distribute H.C. Olive oils according to product protection conditions, both in terms of ambient temperature, exposure to light, especially in the sun and of course the temperature of the product throughout its "life", not to exceed 25^0C. (ideal storage conditions ~ 18^0C). Distribution during the summer months or when passing through tropical areas, to be done with a "refrigerator" vehicle.

Laboratory

Measurements of phenolic, organoleptic, chemical, etc. characteristics will take place. The certification of laboratories for the measurements means acceptance by the interested parties of the methods and protocols of measurement, according to the results of the three Research Bodies of the ARISTOIL program. Otherwise, the measurement process must be approved by the respective accreditation body of its country (NSS).

Research Bodies

The scope of the Cluster is to embrace those Research Institutions that deal with Olive Oil Hygiene Protection Research and would like to own and bear the “ARISTOIL CLUSTER” brand.

Local governmental and social organisations

They are the bodies that are interested in the promotion of the health protection olive oil and contribute in any way to the production and distribution of the product.

Certification

The certification of non-productive-commercial bodies is done through simple procedures /steps, such as:

1. Application,
2. Acceptance by the Board of Directors of the Cluster, and
3. Statement / Commitment of the interested party, that he will comply with the requirements of cluster.

Organisational Structure

The organizational structure has the meaning of Pyramid. In each country, producer groups are established with the main object of producing H.C. olive oil, either autonomously or within existing olive-growing cooperatives. At the same time, there are individual producers-standardizers

The above bodies create a Union, at the national level. The organizations - associations of the countries constitute the MEDITERRANEAN CLUSTER which will have a Legal Form (economic entity) recognized by the EU. (The European Economic Group is set as an example). The organization at all levels would be governed by the rules of QUALITY, DEMOCRACY and REPRESENTATIVE (QDR)

2 Consortium

ARISTOIL CAPITALIZATION

ΙΔΡΥΜΑ ΚΡΑΤΙΚΩΝ ΥΠΟΤΡΟΦΙΩΝ IKY

Erasmus+

This project is funded by the European Union.

Partners from Greece, Turkey and Italy capitalize the outcome of the Interreg output and prepare the training material for stakeholders.

Case Studies

LIVA olive groves in Greece, produce exclusively hygienic olive oil, with environmentally friendly methods of cultivation, harvesting, cold-pressed mechanical production, standardization and handling of olive oil.

Olive oil phenols help protect blood lipids from oxidative stress. The complex of olive oil, olive oil and derivatives contained in olive oil with a concentration> 250mg / Kg, have protective properties for our health and have a positive effect on the prevention of heart attacks, the treatment of inflammation, and recent studies have shown that human Alzheimer's disease and a number of other diseases (see STUDIES, www.livagroves.com/pdf/viologikes-draseis-polyfainolon.pdf). According to the studies several biological activities / effects are described:

1. Olive-Oil-Derived Oleocanthal Enhances ß-Amyloid Clearance as a Potential Neuroprotective Mechanism against Alzheimer's Disease: In Vitro and in Vivo Studies
Abuznait et al with this study provide in vitro and in vivo evidence for the potential of oleocanthal to enhance Aß clearance from the brain via up-regulation of P-glycoprotein (P-gp) and LDL lipoprotein receptor related protein-1 (LRP1), major Aß transport proteins, at the blood-brain barrier (BBB). Results from in vitro and in vivo studies demonstrated similar and consistent pattern of oleocanthal in controlling Aß levels. In cultured mice brain endothelial cells, oleocanthal treatment increased and LRP1 protein expression and activity. Studies showed that administration of oleocanthal to C57BL/6 wild-type mice resulted in Aß clearance from the brain and increased the brain efflux index from 62.0 % for control mice to 79.9% for oleocanthal treated mice. Increased P-gp and LRP1 protein expression in the brain microvessels and inhibition studies confirmed the role of up-regulation of these proteins in enhancing Aß clearance after oleocanthal treatment, which leads to Aß degradation. In conclusion, these findings provide experimental support that potential reduced risk of AD associated with extra-virgin olive oil could be mediated by enhancement of Aß clearance from the brain.

2. Alzheimer's-associated Aß oligomers show altered structure, immunoreactivity and synaptotoxicity with low doses of oleocanthal
This study of Pitt et al has focused on oleocanthal (OC), as a compound capable of altering the assembly state of soluble oligomers of amyloid-ß1-42 peptide (ADDL), which peptide is a neurotoxin that causes Alzheimer's disease (AD). OC increased the immunoreactivity of soluble Aß species, indicating changes in oligomer structure. Analysis of oligomers in the presence of OC showed an upward shift in molecular weight and a ladder-like distribution of SDS-stable ADDL subspecies. In comparison with control ADDLs, oligomers formed in the presence of OC (Aß-OC) showed equivalent co-localization at synapses but exhibited greater immunofluorescence as a result of increased antibody recognition. The enhanced signal at synapses was not due to increased synaptic binding, as direct detection of fluorescently-labeled ADDLs showed an overall reduction in ADDL signal in the presence of OC. Decreased binding to synapses was accompanied by significantly less synaptic deterioration assayed by drebrin loss. Additionally, treatment with OC improved antibody clearance of ADDLs. These results indicate oleocanthal is capable of altering the oligomerization state of ADDLs while protecting neurons from the synaptopathological effects of ADDLs and suggest OC as a lead compound for development in AD therapeutics.

3. Modulation of tau protein fibrillization by oleocanthal

Oleocanthal is capable of altering the fibrillization of tau protein, which is one of the key factors at the basis of neurodegenerative diseases, and of covalently reacting with lysine amino groups of the tau fragment K18 in an unspecific fashion. In the present study, Monti et al investigated the recognition process and the reaction profile between oleocanthal and the wild-type tau protein. As a result, oleocanthal has been found to interact with tau441, inducing stable conformational modifications of the protein secondary structure and also interfering with tau aggregation. These findings provide experimental support for the potential reduced risk of AD and related neurodegenerative diseases associated with olive oil consumption and may offer a new chemical scaffold for the development of AD modulating agents.

4. Inhibition of tau fibrillization by oleocanthal via reaction with the amino groups of tau

In Alzheimer's disease and related tauopathies, tau fibrillizes and aggregates into neurofibrillary tangles. Unpublished data of Li et al indicate an inhibitory effect of oleocanthal on Aß fibrillization, so I was reasoned that oleocanthal might inhibit tau fibrillization as well. Herein it is demonstrated that oleocanthal abrogates fibrillization of tau by locking tau into the naturally unfolded state. Using PHF6 peptide consisting of the amino acid residues VQIVYK, a hexapeptide within the third repeat of tau that is essential for fibrillization, it was shown that oleocanthal forms an adduct with the lysine via initial Schiff base formation. Structure and function studies demonstrate that the two aldehyde groups of oleocanthal are required for the inhibitory activity. These two aldehyde groups show certain specificity when titrated with free lysine and oleocanthal does not significantly affect the normal function of tau. These findings provide a potential scheme for the development of novel therapies for neurodegenerative tauopathies.

5. Oleocanthal Enhances Amyloid-ß Clearance from the Brains of TgSwDI Mice and in Vitro across a Human Blood-Brain Barrier Model

In the current study, Hisham et al investigated the effect of oleocanthal on pathological hallmarks of Alzheimer's disease in TgSwDI, an animal model of AD. Mice treatment for 4 weeks with oleocanthal significantly decreased amyloid load in the hippocampal parenchyma and microvessels. This reduction was associated with enhanced cerebral clearance of Aß across the blood-brain barrier (BBB). Further mechanistic studies demonstrated oleocanthal to increase the expression of important amyloid clearance proteins at the BBB including Pglycoprotein and LRP1, and to activate the ApoE-dependent amyloid clearance pathway in the mice brains. The anti-inflammatory effect of oleocanthal in the brains of these mice was also obvious where it was able to reduce astrocytes activation and IL-1ß levels. Finally, we Hisham et al could recapitulate the observed protective effect of oleocanthal in an in vitro human-based model, which could argue against species difference in response to oleocanthal. In conclusion, findings from in vivo and in vitro studies provide further support for the protective effect of oleocanthal against the progression of AD.

6. Oleocanthal-rich extra virgin olive oil demonstrates acute anti-platelet effects in healthy men in a randomized trial

The phenolic profiles of extra virgin olive oils (EVOOs) may influence their cardiovascular benefits. In a randomized crossover of acute EVOO intake on platelet function, participants (n = 9) consumed 40 mL of EVOO weekly. EVOOs were matched for total phenolic content and were either tyrosol-poor with 1:2 oleacein/oleocanthal (D2i0.5), or 2:1 oleacein/oleocanthal (D2i2), or predominantly tyrosol

(D2i0). Ibuprofen provided a platelet inhibition control. Blood was collected pre- and 2 h post-EVOO intake. D2i0.5 and D2i2 reduced 1 mg/mL collagen-stimulated maximum platelet aggregation (Pmax), with effects best correlated to oleocanthal intake (R = 0.56, P = 0.002). Total phenolic intake was independently correlated to eicosanoid production inhibition, suggesting that cyclooxygenase blockade was not responsible for the Pmax inhibition. Five participants exhibited >25% ΔPmax declines with D2i0.5 and D2i2 intake and plasma metabolomic profiles discriminated subjects by oil responsivity. Platelet responses to acute EVOO intake are associated with oil phenolic composition and may be influenced by diet.

7. Phytochemistry: ibuprofen like activity in extra virgin olive oil.

Newly pressed extra virgin olive oil contains oleocanthal a compound whose pungency induces a strong stinging sensation in the throat, not unlike that caused by solutions of the nonsteroidal anti-inflammatory drug ibuprofen. In the study of Beauchamp et al., 2005, this similar perception seems to be an indicator of a shared pharmacological activity, with oleocanthal acting as a natural anti-inflammatory compound that has a potency and profile strikingly similar to that of ibuprofen. Although structurally dissimilar, both these molecules inhibit the same cyclooxygenase enzymes in the prostaglandin biosynthesis pathway. Both enantiomers of oleocanthal, exhibited a dose-dependent inhibition of COX-1 and COX-2 activities, with no effect on lipoxygenase activity, much as observed with ibuprofen.

8. (-) Oleocanthal as a cMet inhibitor for the control of metastatic breast and prostate cancers

(-) Oleocanthal is a naturally occurring minor secoiridoid isolated from extra virgin olive oil, which showed potent anti-inflammatory activity. In the study of Enagar et al, Computer Assisted Molecular Design (CAMD) identified oleocanthal as a potential virtual cMet inhibitor hit. In this study oleocanthal inhibited the proliferation, migration, and invasion of the epithelial human breast and prostate cancer cell lines with an IC(50) of 4.47μM. Moreover, oleocanthal inhibited the phosphorylation of cMet kinase in vitro, with an IC (50) value of 4.8μM. These results show that oleocanthal and EVOO can have potential therapeutic use for the control of cMet-dependent malignancies.

9. (-)-Oleocanthal inhibits growth and metastasis by blocking activation of STAT3 in human hepatocellular carcinoma

In the present study was explored by Pei et al, the anti-cancer capacity of oleocanthal in human hepatocellular carcinoma (HCC). Oleocanthal inhibited proliferation and cell cycle progression and induced apoptosis in HCC cells in vitro and suppressed tumor growth in an orthotopic HCC model. Oleocanthal also inhibited HCC cell migration and invasion in vitro and impeded HCC metastasis in an in vivo lung metastasis model. Oleocanthal acted by inhibiting epithelial-mesenchymal transition (EMT) through downregulation Twist, a protein which is a direct target of the transcription factor STAT3. Oleocanthal also reduced STAT3 nuclear translocation and DNA binding activity, ultimately downregulating its downstream effectors, including the cell cycle protein Cyclin D1, the anti-apoptotic proteins Bcl-2 and survivin, and the invasion-related protein MMP2. Overexpression of constitutively active STAT3 partly reversed the anticancer effects of oleocanthal, which inhibited STAT3 activation by decreasing the activities of JAK1 and JAK2 and increasing the activity of SHP-1. These data suggest that oleocanthal may be a promising candidate for HCC treatment.

10. (-)-Oleocanthal rapidly and selectively induces cancer cell death via lysosomal membrane permeabilization

LeGendre et al investigated the effect of oleocanthal (OC) on human cancer cell lines in culture and found that OC induced cell death in all cancer cells examined as rapidly as 30 minutes after treatment. OC treatment of non-transformed cells suppressed their proliferation but did not cause cell death. OC induced both primary necrotic and apoptotic cell death via induction of lysosomal membrane permeabilization (LMP). Here evidence are provided showing that OC promotes LMP by inhibiting acid sphingomyelinase (ASM) activity, which destabilizes the interaction between proteins required for lysosomal membrane stability. The data presented here indicate that cancer cells, which tend to have fragile lysosomal membranes compared to non-cancerous cells, are susceptible to cell death induced by lysosomotropic agents. Therefore, targeting lysosomal membrane stability represents a novel approach for the induction of cancer-specific cell death.

11. Cytotoxic Activity of Oleocanthal Isolated from Virgin Olive Oil on Human Melanoma Cells

Oleocanthal's potential anticancer activity has already been reported but only limited evidence has been provided in cutaneous malignant melanoma. The present study of Fogli S et al is aimed at investigating the selective in vitro antiproliferative activity of oleocanthal against human malignant melanoma cells. Cell viability experiments demonstrated that oleocanthal had a remarkable and selective activity for human melanoma cells versus normal dermal fibroblasts with IC50s in the low micromolar range of concentrations. Such an effect was paralleled by a significant inhibition of ERK1/2 and AKT protein phosphorylation and downregulation of the gene Bcl2 expression. These findings may suggest that extra virgin olive oil phenolic extract enriched in oleocanthal deserves further investigation in skin cancer.

12. In Cell Interactome of Oleocanthal, an Extra Virgin Olive Oil Bioactive Component.

Cassiano C et al revealed in their research via chemical proteomics that heatshock proteins, HSP70 and HSP90, as main oleocanthal interactors in living systems. These two proteins are involved in cancer development and, thus, our findings could have important outcomes for a deep evaluation of the biopharmacological significance of oleocanthal.

13. Olive Oil-derived Oleocanthal as Potent Inhibitor of Mammalian Target of Rapamycin: Biological Evaluation and Molecular Modeling Studies

Mammalian target of rapamycin (mTOR) is a protein that integrates signals from energy homeostasis, metabolism, stress response, and cell cycle, with reported role in cancer and Alzheimer's disease development. This function encouraged the team of Mohammad A. Khanfar et al to examine the possibility that oleocanthal inhibits mTOR. Subsequent experimental validation indicated that oleocanthal indeed inhibited the enzymatic activity of mTOR with an IC50 value of 708 nM. Oleocanthal inhibits the growth of several breast cancer cell lines at low micromolar concentration in a dose-dependent manner. Oleocanthal treatment caused a marked downregulation of phosphorylated mTOR in metastatic breast cancer cell line (MDA-MB-231). These results strongly indicate that mTOR inhibition is at least one of the factors of the reported anticancer and neuroprotective properties of oleocanthal.

14. Olive Phenolics as c-Met Inhibitors: (-)-Oleocanthal Attenuates Cell Proliferation, Invasiveness, and Tumor Growth in Breast Cancer Models

Dysregulation of the Hepatocyte growth factor (HGF)/c-Met signaling axis upregulates diverse tumor cell functions, including cell proliferation, survival, scattering and motility, epithelial-to-mesenchymal transition (EMT), angiogenesis, invasion, and metastasis. The aim of this study was to characterize the intracellular mechanisms involved in mediating the anticancer effects of (-)-oleocanthal treatment and the potential involvement of c-Met receptor signaling components in breast cancer. Results showed that (-)-oleocanthal inhibits the growth of human breast cancer cell lines MDA-MB-231, MCF-7 and BT-474 while similar treatment doses were found to have no effect on normal human MCF10A cell growth. In addition, (-)-oleocanthal treatment caused a dose-dependent inhibition of HGF-induced cell migration, invasion and G1/S cell cycle progression in breast cancer cell lines. Moreover, (-)-oleocanthal treatment effects were found to be mediated via inhibition of HGF-induced c-Met activation and its downstream mitogenic signaling pathways. This growth inhibitory effect is associated with blockade of EMT and reduction in cellular motility. Further results from in vivo studies showed that (-)-oleocanthal treatment suppressed tumor cell growth in an orthotopic model of breast cancer in athymic nude mice. Collectively, the findings of this study suggest that (-)-oleocanthal is a promising dietary supplement lead with potential for therapeutic use to control malignancies with aberrant c-Met activity.

15. Effect of Oleocanthal and Its Derivatives on Inflammatory Response Induced by Lipopolysaccharide in a Murine Chondrocyte Cell Line

In joint diseases, cartilage homeostasis is disrupted by mechanisms that are driven by combinations of biologic factors. Osteoarthritis progression is characterized by increased nitric oxide (NO) production, which has been associated with cartilage degradation. Oleocanthal displays antiinflammatory drug activity similar to that of ibuprofen, a drug widely used in the therapeutic management of joint inflammatory diseases. In this study Iacono et al evaluated the effect of oleocanthal and its derivatives on the modulation of NO production in chondrocytes. Oleocanthal and its derivatives decreased lipopolysaccharide-induced NOS2 synthesis in chondrocytes without significantly affecting cell viability at lower concentrations. Among the derivatives that were examined, derivative 231 was the most interesting, since its inhibitory effect on NOS2 was devoid of cytotoxicity even at higher concentrations. This class of molecules shows potential as a therapeutic weapon for the treatment of inflammatory degenerative joint diseases.

16. Effects of olive oil polyphenols on erythrocyte oxidative damage.

In this work, Pavla-Martins et al studied the capacity of oleacin to protect red blood cells (RBCs) from oxidative injury. The in vitro oxidative stress of RBCs was induced by the water-soluble radical initiator 2,2'azobis (2amidinopropane) dihydrochloride and changes were evaluated either by optical microscopy or by the amount of hemolysis. Oleacein was shown to significantly protect RBCs from oxidative damage in a dose-dependent manner. Oleacein had the most powerful effect at 20mM, within the other polyphenols. Even at 3mM, oleacein still had an important protective activity. For the first time it was demonstrated that oleacein may play a noteworthy protective role against ROS-induced oxidative injury in human cells since lower doses of this compound were needed to protect RBCs in vitro from oxidative mediated hemolysis.

17. Oleacein. Translation from Mediterranean Diet to Potential Antiatherosclerotic Drug

Oleacein, due to its abundance, in olive oil, it may play a special role in decreasing the progression of atherosclerosis. Some bioactivities of oleacein, such as antioxidant, anti-inflammatory, anti-

proliferative and antimicrobial, were documented. There is also evidence of the bioavailability of oleacein in humans as well. However, due to the lack of clinical data, further studies are needed to provide information about the usefulness of this compound in antiatherosclerotic therapy.

18. Oleacein enhances anti-inflammatory activity of human macrophages by increasing CD163 receptor expression.

Filipek et al examined whether oleacein could increase CD163 and IL10 receptor expression as well as intracellular secretion of protein heme oxygenase 1 (HO1) in human macrophages. Effect of oleacein (10 and 20 μmol/l) or oleacein together with complexes of haemoglobin (Hb) and haptoglobin 11 (Hp11) or haptoglobin 22 (Hp22) on expression of IL10 and CD163 receptors was determined by Flow Cytometry. HO1 intracellular secretion in macrophages was investigated by enzyme-linked immunosorbent assay (ELISA). Oleacein together with complexes HbHp11 or HbHp22 stimulated the expression of CD163 (30-100 fold), IL10 (170-300 fold) and HO1 secretion (60-130 fold) after 5 days of co-incubation. Our results suggested that oleacein enhances anti-inflammatory activity of complexes haemoglobin with haptoglobin 11 and 22 and could play a potential role in the prevention of inflammatory disease related to atherosclerosis.

19. Oleuropein and oleacein may restore biological functions of endothelial progenitor cells impaired by angiotensin II via activation of Nrf2/heme oxygenase1 pathway.

Oleacein was examined if is able to protect Endothelial progenitor cells EPCs against impairment of their functions due to angiotensin-induced cell senescence. CD31(+)/VEGFR2(+) cells were cultured with angiotensin in presence or absence of increasing concentrations (from 1.0 to 10.0 μM) of oleacein. As compared to angiotensin II-treated cells, EPCs exposed to oleacein prior to angiotensin II showed a significant increase of proliferation and telomerase activity, and a decrease in the percentage of senescent cells and intracellular ROS formation. Oleacein restored migration, adhesion and tube formation of EPCs diminished by angiotensin II in a concentration-dependent manner. This effect was related to NFE2-related factor 2 (Nrf2) transcription factor activation and the increase of heme oxygenase1 (HO1) expression.

20. One-step semisynthesis of oleacein and the determination as a 5-lipoxygenase inhibitor.

5-lipoxygenase is a direct target for oleacein with an inhibitory potential (IC50: 2 μM) more potent than oleocanthal and oleuropein. This enzyme catalyzes the initial steps in the biosynthesis of pro-inflammatory leukotrienes. This investigation presented here an alternative solution to isolation or total synthesis for the procurement of oleacein, thus facilitating the further development as a potential anti-inflammatory agent.

21. Olive secoiridoids and semisynthetic bioisostere analogues for the control of metastatic breast cancer.

In the study of Busnena et al, ligstroside aglycone showed the best antimigratory activity against the highly metastatic human breast cancer cell line MDAMB231. Generally, tyrosol esters showed better activities versus carbamate analogues. Tyrosol esters with a phenolic acid containing hydrogen bond donor and/or acceptor groups at the para-position have better anticancer and c-MET protein inhibitory activities. Olive oil secoiridoids, like ligstroside aglycon, are excellent scaffolds for the design of novel c-MET inhibitors.

22. tabAnti-HER2 (erbB-2) oncogene effects of phenolic compounds directly isolated from commercial Extra-Virgin Olive Oil (EVOO)

Menendez et al in their study explored the ability of ligstrocide aglycon to modulate HER2 tyrosine kinase receptor-induced in vitro transformed phenotype in human breast epithelial cells. Using MCF10A normal breast epithelial cells it was further determined the relationship between chemical structure of ligstrocide aglycon and its inhibitory activities on the tyrosine kinase activity of the HER2 oncoprotein. When compared with untreated cells, MCF10A/HER2 cells, treated with ligstroside aglycone, grew less dense, were significantly bigger in volume and showed a profound reorganization of cell-cell contacts with the appearance of multiple extrusions. Ligstroside aglycone was one of the most active inhibitors of HER2 expression in MCF10A/HER2 cells, with a reduction 68%, and IC50 10μM. HER2 overexpression further promoted an exacerbated sensitivity to the apoptotic effects of ligstroside aglycone. These findings molecularly support epidemiological evidence revealing that lingstrocide aglycon anti-breast cancer effects primarily affect the occurrence of breast tumors overexpressing the type I receptor tyrosine kinase HER2 but further suggest that its stereochemistry might provide an excellent and safe platform for the design of new HER2 targeted anti-breast cancer drugs.

23. The Polyphenol Oleuropein Aglycone Protects TgCRND8 Mice against Aß Plaque Pathology

In their research, Grossi et al used the double transgenic TgCRND8 mice, which overexpressing the Swedish and Indiana mutations in the human amyloid precursor protein, to examine in vivo the effects of 8 weeks dietary supplementation of oleuropein aglycone at the dose of 50 mg/kg. The dietary supplementation of oleuropein aglycone strongly improves the cognitive performance of young/ middle-aged TgCRND8 mice. Immunofluorescence analysis of cerebral tissue in these mice showed remarkably reduced ß-amyloid levels and plaque deposits. Moreover, microglia migration to the plaques for phagocytosis and a remarkable reduction of the astrocyte reaction were evident. Finally, oleuropein aglycone-fed mice brain displayed an astonishingly intense autophagic reaction, as shown by the increase of autophagic markers expression and of lysosomal activity. Data obtained with cultured cells confirmed the latter evidence, suggesting mTOR regulation by oleuropein aglycone. These results support, and provide mechanistic insights into, the beneficial effects against Alzheimer-associated neurodegeneration of oleuropein aglycone.

24. Oleuropein aglycon prevents cytotoxic amyloid aggregation of human amylin

Here, Rigacci S. et al investigated the effects on amylin aggregation and cytotoxicity of the oleuropein aglycon. It was showed that oleuropein, when present during the aggregation of amylin, consistently prevented its cytotoxicity to RIN-5F pancreatic ß-cells, as determined by the 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide test and caspase-3 activity assay. A lack of interaction with the cell membrane of amylin aggregates grown in the presence of oleuropein was shown by fluorescence microscopy and synthetic lipid vesicle permeabilization. Moreover, the ThT assay, circular dichroism analysis and electron microscopy images suggested that oleuropein interferes with amylin aggregation, resulting in a different path skipping the formation of toxic prefibrillar aggregates. These results provide a molecular basis for some of the benefits potentially coming from extra virgin olive oil consumption and pave the way to further studies on the possible pharmacological use of oleuropein to prevent or to slow down the progression of type II diabetes.

25. Extra-virgin olive oil polyphenols inhibit HER2 (erbB-2)-induced malignant transformation in human breast epithelial cells: Relationship between the chemical structures of extra-virgin olive oil secoiridoids and lignans and their inhibitory activities on the tyrosine kinase activity of HER2
Menendez et al in their study explored the ability of oleuropein aglycon to modulate HER2 tyrosine kinase receptor-induced in vitro transformed phenotype in human breast epithelial cells. Using MCF10A normal breast epithelial cells it was further determined the relationship between chemical structure of oleuropein aglycon and its inhibitory activities on the tyrosine kinase activity of the HER2 oncoprotein. When compared with untreated cells, MCF10A/HER2 cells, treated with oleuropein aglycone, grew less dense, were significantly bigger in volume and showed a profound reorganization of cell-cell contacts with the appearance of multiple extrusions. Oleuropein aglycone was one of the most active inhibitors of HER2 expression in MCF10A/HER2 cells, with a reduction 63%, and IC50 64μM. HER2 overexpression further promoted an exacerbated sensitivity to the apoptotic effects of oleuropein aglycone. These findings molecularly support epidemiological evidence revealing that oleuropein aglycon anti-breast cancer effects primarily affect the occurrence of breast tumors overexpressing the type I receptor tyrosine kinase HER2 but further suggest that its stereochemistry might provide an excellent and safe platform for the design of new HER2 targeted anti-breast cancer drugs.

Good agricultural and manufacturing practice (GAMP) can help to preserve as well as improve polyphenolic substances and hence the quality of the product. Thanks to their health properties, these substances can increase the perceived value of the product (Boncinelli et al 2016, Clodoveo et al 2016).

Health claims can be used for the designing comprehensive labelling to increase consumers' knowledge about the product quality. It can provide competitive advantages as well as the added value for consumers. On the other hand, health claims are a rarely applied legal tool for olive oil (European Commission, 2006). It has been stated that the higher usage of such health claims may decrease the difference between the perceived and actual value of EVOO. Furthermore, such a health claim also provides information about healthy properties of EVOO resulting in higher demand for the same quality level (Coppola and De Stefano 2000, Roselli et al 2017). Researchers have also reported that using such a label system containing the health claim about EVOO polyphenols content may also provide “healthiest” EVOO while giving the “highest quality” (Roselli et al 2017). In case studies, there is evidence showing consumers' willingness to pay a premium price for the health-enhancing characteristics of food (Bimbo et al., 2016; Nocella & Kennedy, 2012). In addition, a few studies have shown that some consumers' segments are willing to buy the best products and to pay a higher price for EVOOs with health claims (Boncinelli et al., 2016; Casini et al., 2014). As a result, EVOO industry can use the approved health claim as an advantage to increase their income while serving healthy nutritious products to public.

All players in the supply chain should combine their efforts to increase the supply of products having the highest quality with the greatest health benefits. At same time, it is critical to develop innovative and persuasive communication strategies to raise consumers' awareness about the quality and their willingness to pay a premium price to guarantee a fair income for high quality EVOO producers. In this perspective, health claims can be used as an available tool to segment the wide and heterogeneous EVOO trade category. In particular, the health claim about polyphenol content of EVOO can decrease

consumers' information asymmetry about the product. Such a health claim can also create an added value in the olive growing sector, while proving better coordination in the supply chain between farmers, millers, packers as well as distributors (Roselli et al 2017).

It is possible to find a noticeable supply variation in traditional foods on the market, especially with respect to the credence attributes such as designation of origin, organic certification, and health claims. The health claim has been reported as more effective than protected designation of origin and organic labels on the choices of several types of consumers (Boncinelli et al 2016). Thus, products having the health claim meet the growing interest of consumers (Roosen et al 2007, Verbeke et al 2009).

It has been shown that healthiness, along with taste, represent one of the principal purchasing motivations of EVOO (Santosa et al 2013). Thus, supplying of products having EVOO with health claims can bring local and international competitiveness. For various products including EVOO, health claims have shown to have a distinctly positive impact on choices of consumer (Roosen et al 2007, Verbeke et al 2009).

EVOO with health claim should be a positive virtue of healthy diet. Some mostly used parameters for the categorization of EVOO such as acidity level or sensory characteristics is not enough to show its quality or health benefits. Therefore, the health claim for EVOO has recently gained interest as indicator of the overall quality for the consumers. EVOO with health claim can also be thought as a tool to serve public health by prevention of diseases and supporter immune system.

The production of EVOO with high content phenols will reduce the phenol content of waste-water. This makes easier purification of waste-water and reduces its pollution effects on environment. Thus, production EVOO with health claims can also present environmental benefits. People who have entrepreneurs and a high education level also migrates from city to rural for the production EVOO with health claim. This reduces unemployment both in the countryside and the village. These producers have knowledge about the importance of high quality EVOO for economy, health and social development. They design their EVOO production in this concept. By this way, they create a new employment area in rural and they also motivate the older or local producers to produce EVOO with health claim. They also transfer the culture of modern working idea by using innovative tools in production.

Some examples of case studies can be summarized as follows:

One electric engineer from one international company migrated from a big city center to rural region of south-west side of Turkey and he started to grow olive and produced EVOO in his own company. He used the modern cultivation and processing techniques. He also started to sell his EVOO with health claim to big cities with considerable prices and he encouraged the neighborhood farmers and producers to produce high quality of product.

Another similar story belongs to an engineer who also moved south-east side of Turkey for production high quality EVOO with health claim. He cultivated olives in their family orchard with his family

according to modern cultivation and harvesting techniques to obtain EVOO with high phenol content. The family processed their olives in a milling plant in same region and they packed their EVOO in dark bottle. Their company has been reported as the first company which managed to export EVOO. After then, other olive farmers and processors were inspired to produce EVOO having high phenol content.

Another similar success story is about an advocate for high phenol EVOO production. He is from the biggest city of Turkey but he had established an olive orchard in south-east side of Turkey. Healthy olives had been cultivated and harvested during green ripening step after then the olives had been processed for the production of oil. Chemical analysis obtained from oils had reflected high phenol content of EVOO. Based on this story new employments were showed up, high value EVOOs were produced and sold to metropolitan cities, consumers from EVOOs producing cities can obtain EVOO with health claim at reasonable price. Because of this success story, other farmers/producers took this story as an example and they also started to work to obtain high phenol EVOO.

A group of young people from urban life invested a partnership to olive growing sector and EVOO production sector in rural area. They created new working areas such as cultivation, harvesting and transportation etc. for rural citizen. They also give training to your worker and other local farmers/producers about the difference of ordinary olive oil and EVOO with health claim. They produce EVOO with health claim and sell their products by using good and informative communication via online advertisement, social media and web pages. This creates an awareness about both productions of high quality EVOO and the importance of online facilities on consumers.

A notary in metropolis established new olive orchards to produce EVOO. He had taken courses about the quality of EVOO and olive growing with modern and ecologic cultivation techniques. Then, he decided to produce high quality EVOO with health claim. For this purpose, he was also trained for his workers. As a result of training and his application for GAMP, he received EVOO product awards in national and international EVOO competitions. Also, his firm also reduced the pollution effects of cultivation and processing. He created an awareness of EVOO with health claim and environmental protection in production in rural areas of the city. As a result, similar ideas for high quality EVOO production were increased in near regions.

Another story is about a pharmacist who wanted to generalize the benefits of EVOO with health claim to wide public. She started grow olives in an orchard and then she processed olives to oil immediately after the harvesting of healthy olives. She educated to consumers about the beneficial effects of high phenol EVOO and the differences between the ordinary olive oil and high phenol containing EVOO. Consequently, a high awareness was raised among consumers and then they started to prefer to consume high phenol EVOO.

The collection of case studies about production of EVOO with health claim resulted in;

- An attractive investment area for especially intellectual enterprises or professionals
- New trend for old olive farmers as well as EVOO producers
- Increased migration of professionals from metropolitans or from urban to rural resulting in reduces in the unemployment ratio of urban

- Development of new working places in rural. This also reduces the migration of rural workers to urban areas and hence decreases in unemployment in urban
- Increases in the facilities of education and places for training of rural worker/farmer/producer
- Establishment and development of new advertising, communicating and marketing channels for rural
- Creating awareness about high quality product with same production cost but high income
- Transferring of intellectual knowledge and experience from professional workers of metropolitan city to the rural farmers/producers
- Creating awareness of consumers for selection of EVOO with high health benefits
- Using of the environment friendly production techniques such as GAMP and pollutant content reducing technique of waste-water
- Increasing of local and international competitiveness
- Increasing of environmental benefits

This collection of case studies about the use of health claims have showed that the production EVOO with health claim brings competitiveness as well as economical, health and environmental benefits at local and worldwide levels. The use of health claims offers these benefits in multiple ways such as reducing environmental pollution, increasing employability, increasing social communication tools, reducing health expenditures of consumers, increasing awareness of scientific results about EVOO production technology, EVOO characteristics and its health effects. The quantification of this benefit and the collection of case studies give a proof of concept for stakeholders about its usefulness.

Phenols in LIVA olive groves are measured in specialized laboratories with the most reliable ones being based on NMR methodology, where the nuclear spectrometer analyzes all phenols and their size. The sum of phenols, tyrosol derivatives and hydroxytyrosol is denoted by D3 (Davis ...). Clinical trials use olive oils with a specific D3 value. So, since not all olive oils are the same, all olive oils that qualify for Health Claim (D3> 250mg / Kg) must be categorized according to D3.

OLIVE LIVES, to serve the consumer, classify olive oils into five categories, depending on the phenol content.

There are five (5) defined categories depending on the content:

1. DIAMOND D3> 1000mg / Kg
2. PLATINUM D3> 600mg / Kg
3. GOLD D3> 350mg / Kg
4. SILVER D3> 250mg / Kg
5. CLASSIC D3> 200mg / Kg

The first three are designated HEALTH CLAIM and the other two are designated HEALTH PHILOSOPHY.

According to European Regulation 432/2012 (L 136 / 25.5.2012 p. 26), the Health Claim - can only carry olive oil containing at least 250 mg of polyphenols per 1 kg of olive oil. The product of the liva olive oil series goes well beyond this limit (see Certificate), and is certified by Health Claim.

Olive oil polyphenols help protect blood lipids from oxidative stress. The complex of olive oil, olive oil and derivatives contained in the olive oil with the above concentration, have protective properties for our health and have a positive effect on the prevention of heart attacks, in the treatment of inflammation, and recent studies have shown that Alzheimer's.

Based on the certification of the concentration of polyphenols in our olive oil, the beneficial results are ensured by the recommended daily intake of 20g of olive oil. An analysis certificate in Greek only could be seen in the following link: www.livagroves.com/pdf/DIAMOND_18_GR.pdf

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