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- Introduction to Innovative Food Processing and Technology
- High intensity sweeteners chemicals structure, properties and applications
- Side effects of the Antioxidants over the Cancer Therapy
- Associations between nutritional composition and farming type of organically and conventionally grown cereals

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## Introduction to Innovative Food Processing and Technology

Ozlem Tokusoglu<sup>1\*</sup>

Consumers around the world are better educated and more demanding in their identification and purchase of quality health-promoting foods. The food industry and regulatory agencies are searching for innovative technologies to provide safe and stable foods for their clientele. Thermal pasteurization and commercial sterilization of foods provide safe and nutritious foods that, unfortunately, are often heated beyond a safety factor that results in unacceptable quality and nutrient retention. Nonthermal processing technologies offer unprecedented opportunities and challenges for the food industry to market safe, high quality health-promoting foods. The development of nonthermal processing technologies for food processing is providing an excellent balance between safety and minimal processing, between acceptable economic constraints and superior quality, and between unique approaches and traditional processing resources (6). Nonthermal food processing is often perceived as an alternative to thermal food processing, yet there are many nonthermal preparatory unit operations as well as food processing and preservation opportunities and challenges that require further investigation by the food industry. Nonthermal technologies are useful not only for inactivation of microorganisms and enzymes, but also to improve yield and development of ingredients and marketable foods with novel quality and nutritional characteristics (1,4,5).

Nonthermal processing is effectively combined with thermal processing to provide improved food safety and quality. Nonthermal processing facilitates the development of innovative food products not

Previously envisioned. Niche markets for food products and processes will receive greater attention in future years. Nonthermal technologies successfully decontaminate, pasteurize, and potentially pursue commercial sterilization of selected foods while retaining fresh-like quality and excellent nutrient retention. The quest for technologies to meet consumer expectations with optimum quality safe processed foods is a most important priority for future food science research. Zhang et al. (2011) listed the relevant factors to consider when conducting research into novel nonthermal and thermal technologies as: 1) target microorganisms to provide safety; 2) target

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(Associate Professor Dr.) completed her PhD from Ege University in the Department of Food Engineering, Izmir, Turkey. Tokuşođlu was research associate at the Food Science and Nutrition Department at the University of Florida, Gainesville, USA and at the School of Food Science, Washington State University, Pullman, in the State of Washington, USA. Tokuşođlu, is currently also working as associate professor, in Department of Food Engineering of Celal Bayar University.



enzymes to extend quality shelf life; 3) maximization of potential synergistic effects; 4) alteration of quality attributes; 5) engineering aspects; 6) conservation of energy and water; 7) potential for convenient scale-up of pilot scale processes; 7) reliability and economics of technologies; and 8) consumer perception of the technologies. "The search for new approaches to processing foods should be driven, above all, to maximize safety, quality, convenience, costs, and consumer wellness" (4,5,6).

Morris et al. (2007) conclude that nonthermal unit operations in food processing interest food scientists, manufacturers, and consumers because the technologies expose fresh foods to minimal impact on nutritional and sensory qualities, yet presumably provide safe shelf stable foods by inactivating pathogenic microorganisms and spoilage enzymes. The presumption that nonthermal processing is energy efficient and environmentally friendly adds to contemporary popularity.

Additional benefits to the food industry include the provision of food safety, value-added heat labile foods, and new market opportunities.

Nonthermal food processing technologies are extensive with high hydrostatic pressure (HHP), pulsed electric fields (PEF), ultrasonics, ultra-violet light, ionizing irradiation (electron beams) and hurdle technologies leading the way. In addition, pulsed X-rays, pulsed high intensity light, high voltage arc discharge, magnetic fields, dense phase carbon dioxide, plasma, ozone, chlorine dioxide, and electrolysed water are receiving attention individually and as a hurdle in minimal processing protocols (2,3,4,5).

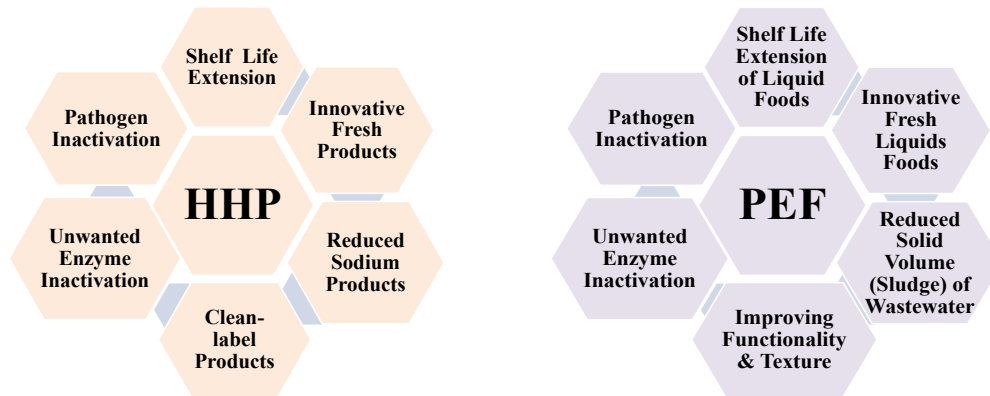


Figure 1. The Usage Area of High Hydrostatic Pressure (HHP) and Pulsed Electrical Field (PEF) (4,5)

Current researches devote attention to improving food functionality with high hydrostatic pressure (HHP) and pulsed electric fields (PEF). The focus on improving the quality and retaining bioactive constituents of fruits and vegetables and improving the quality of dairy, egg, meat and seafood products

with HHP is evident in many chapters. The inclusion of reviews of modelling and simulation of HHP inactivation of microorganisms and the relative effects of HHP processing on food allergies and intolerances broadens the scope of the information provided.

Improving food functionality with pulsed electric field (PEF) processes are focussed on dairy and egg products, fruit juices and wine. A chapter attending to industrial applications of HHP and PEF systems and potential commercial quality and shelf lives of food products concludes this discussion.

High hydrostatic pressure (HHP), ultra-high pressure (UHP), ultra-high pressure processing (HPP) are different names and acronyms for equivalent nonthermal processes employing pressures in the range of 200 to 1000 MPa with only small increases in processing temperature. The ultra-high pressures inactivate microbial cells by disrupting membrane systems, retaining the biological activity of quality, sensory and nutrient cell constituents, thus extending the shelf lives of foods.

High pressures inactivate enzymes by altering the secondary and tertiary structures of proteins, changing functional integrity, biological activity, and susceptibility to proteolysis. HHP processing of dairy proteins reduces the size of casein micelles, denatures whey proteins, increases calcium solubility and induces color changes (2). The use of HHP to increase the yield of cheese curd from milk and accelerate the proteolytic ripening of Cheddar cheeses are promising improvements to the economics for the dairy food industry. The most widely available commercial applications of HHP include pasteurization of quacamole, tomato salsas, oysters, deli sliced meats, and yogurts. The provision of HHP processing to provide a preservation method for thermally labile tropical fruits is very promising.

Pulsed electric field processing (PEF) exposes fluid foods to microsecond bursts of high intensity electric fields, 10 to 100 kV/cm, inactivating selected microorganisms by electroporation, a disruption of cell membranes. PEF processing reliably results in five log reduction in selected pathogenic microorganisms, resulting in minimal detrimental alterations in physical and sensory properties of the fluid foods.

PEF adequately pasteurizes acid ( $\text{pH} < 4.5$ ) fruit juices, and research is continuing on uniform adequate pasteurization of milk and liquid eggs. The commercial application of PEF to improve extraction yield of fruit juices and bioactive components of plant materials are in progress. PEF inactivation of enzymes is inconsistent and non-uniform resulting in plant products subject to short shelf lives at ambient temperatures. Although PEF is identified as a nonthermal process, temperature increases during PEF processing results in fluid foods at 35 to 50°C requiring cooling prior to packaging. The presence of particulates or bubbles in fluid foods subjected to PEF will result in dielectric breakdown, arcing and scorching of the food. Homogenization and vacuum degassing are necessary minimize the hazards associated with PEF processing of fluid foods.

Technical issues that must be addressed to commercialize PEF for approval as an adequate food pasteurization technology include: 1) consistent and uniform generation of high intensity electric fields; 2) identification of critical electric field intensities for uniform microbial inactivation; 3) identification of homogenization and vacuum degassing techniques to assure the absence of particulates and air cells that promote arcing, and 4) identification of flow rates, temperature control, cooling and aseptic packaging parameters to obtain processing uniformity and safe handling practices (2,4,5).

High hydrostatic pressure (HHP) and pulsed electric fields (PEF) processing of foods continues with a focus on heat labile acid fruits, vegetables and dairy foods that meet consumer expectations for a minimally process, safety, fresh-like quality and

convenience. Nonthermal preservation extend shelf life without the addition of preservatives while retaining expected fresh-like appearance, sensory and nutrient quality. It will be necessary to combine nonthermal and thermal preservation technologies to inactivate heat resistant spores potentially contaminating low acid foods. Commercial nonthermal processing success stories such as pasteurized quacamole, oysters, salsa, yogurt and refrigerated meats and improved yields of fruit juices and bioactive compounds from herbs and other plant materials will demonstrate the efficacy and economic success of the technologies in niche markets. Successful research and identification of economic benefits including energy and water conservation as well as demonstrated safety and fresh-like quality attributes will improve consumer perception of nonthermal technologies and result in further development by the food industry around the world.

**Conflict of interests:** We declare that we have no conflict of interests.

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## High intensity sweeteners chemicals structure, properties and applications

Osama Ibrahim<sup>1\*</sup>

### Abstract

High Intense-sweeteners (HIS) are commonly used as a sugar substitutes or sugar alternatives and provide sweet without calories. HIS are in high demands due to its multiple advantages including assisting people in losing weight or avoiding obesity and assisting diabetics to control their blood sugar level. The first known intense-sweetener is Saccharine that was discovered in the year 1878. Since then scientists discovered several other intensive sweeteners that are sweeter than sucrose with zero calorie. Some discovered sweeteners are Plants extract (Steviol glycosides, and Mogrosides), semi-synthetic peptides (Aspartame, Neotame, and sucralose), and synthetic chemicals. (Saccharine, Acesulfame-K, and Cyclamate).

These High intensive sweeteners have been approved as safe for applications (1) in foods, beverages, dietary supplements, and pharmaceuticals products by Food and Drug administration (FDA) (2) in United States and by other similar agencies in other countries (3). The levels of these non-nutritive high intensive sweeteners used in foods, beverages, dietary supplements, and pharmaceutical products are based on the approved daily intake (ADI) by FDA and by other safety authorities worldwide. This ADI level is 100 fold lower than the safe dose demonstrated in laboratory studies. It is estimated that the global demand of HIS is exceeding 9.0 billion dollars and growing. The only HIS that is declining in global market is the old discovered sweetener Saccharine

**Keywords:** High intensive sweeteners, natural sweeteners, artificial sweeteners, Saccharine, Aspartame, Acesulfame-k, Cyclamate, Sucralose, Neotame, Steviol glycosides (Rebaudioside-A), and Tri-terpine glycoside (Mogroside-V)

### Introduction

High Intensive sweeteners (HIS) are commonly used in food products, beverages and some oral pharmaceuticals as sugar substitutes or sugar alternatives (4) All high intensive sweeteners (HIS) are zero calories and hundreds time sweeter than sucrose.

HIS produced from natural sources are recognized by FDA as safe with GRAS status (Generally Recognized As Safe) (4). These HIS with GRAS status does not require FDA approval and can be used in foods and other applications after submitting a GRAS notice to FDA. The GRAS statutes of these HIS are determined as safe because they are naturally occurred in plants or produced from non-pathogenic microorganism. This safety standard of GRAS status are defined in FDA's regulations and scientists must determine that a sweetener with GRAS status meet the safety standard of reasonable certainty no harm to consumers under the intend conditions of its use.

GRAS notices have been submitted to FDA for two types of high-intensity sweeteners.

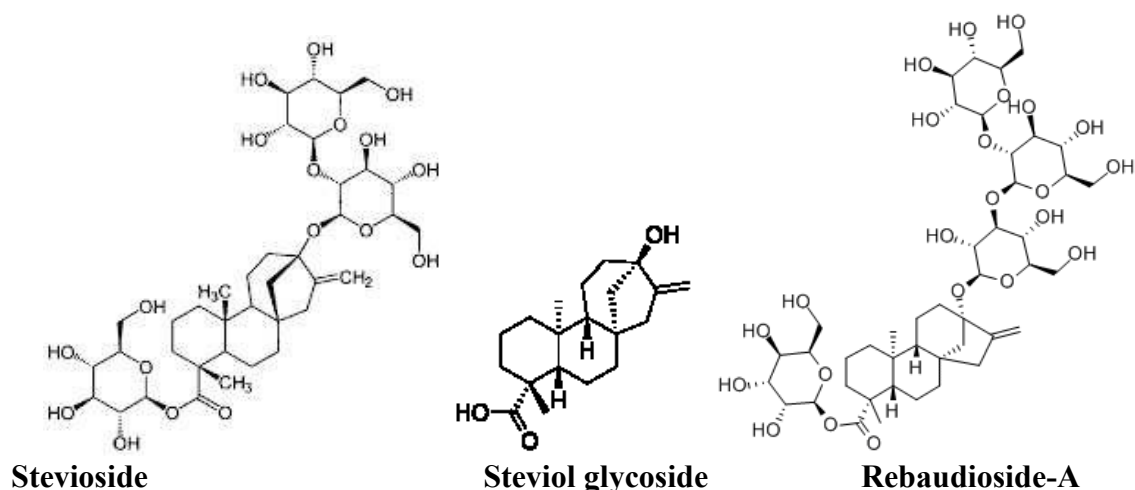
These two types are certain steviol glycosides extracted from the leaves of the stevia plant *Stevia rebaudiana* and mogrosides extracted from Luo Han Guo (Monck fruit) *Siraitia grosvenori* Awingle.

HIS produced from non-natural sources by semi-synthetic or synthetic chemistry process must undergo premarket review and approved by FDA before it can be used as food additives in foods or other applications. The Six high-intensity sweeteners that required such approval by FDA in the United States as food additives are Saccharine, Aspartame, Neotame, Acesulfame K, Sucralose, and Cyclamate

### High intensive sweeteners with GRAS status

These are the two natural High intensive sweeteners of Steviol glycosides and Mogroside that did not require FDA approval because both are extracted from plants and determined as safe. The following are chemicals structure and properties of these two natural high intensive sweeteners (HIS) of Steviol glucosides and Mogrosides

## 1. Steviol glycosides:



Steviol glycosides (5) are natural extract of the leaves of *Stevia rebaudiana* a native plant to part of South America and commonly known by the name *Stevia* (6). Steviol glycosides (7) are non-nutritive zero calorie sweeteners accompanied by after taste and are reported to be 200 to 400 sweeter than sucrose depend on the type of application and formulation.

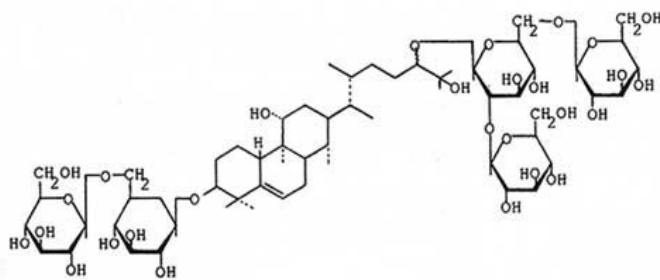
There are two chemical structures of Steviol glycosides extracted from *Stevia* leaves known by the name Stevioside and Rebaudioside-A. Both Stevioside and Rebaudioside-A are the two extracts with intensive sweeteners in the stevia leaf.

In the year 2008, the FDA recognized only Rebaudioside-A, as safe with GRAS status (8) for foods, beverages and other applications. Its acceptable daily intake (ADI) is 4 mg/kg body weight.

The chemical structure of Rebaudioside-A which is also known by the name Reb-A or Rebiana-A has one beta-D-glucose replacing the bottom hydrogen atom of steviol glycoside and a chain of three beta-D-glucose molecules replacing the top hydrogen site of steviol glycoside.

This sweetener Rebaudioside-A (RebA or Rebiana A) is blended with the sugar alcohol erythritol and marketed in United States under trade name Truvia®.

## 2. Mogrosides



**Tri-terpene glycoside (Mogroside-V)**

Mogrosides are extracted from the plant LUO HAN GUO which also known by the name Monk fruit (9). Both names are the common names for the plant *Sarmatia grosvenorii* that is grown predominantly in the southern mountains of Guangxi province, southern China.

Monk Fruit has been cultivated and consumed in China for hundreds of years with no harm to the consumers. It is sold in China as a sweeteners and flavour ingredient for foods and beverages, as well as used in traditional Chinese medicine for hundreds of years.

The fruit is a truly natural, and its extract contains a mixture of five chemical structures known by the name mogrosides. There are five chemicals structure of mogrosides (I, II, III, IV, and V), these numbers are the number of glucose units that are attached to the chemical structure of mogroside unit. All mogrosides are zero calorie sweeteners and 100 to 250 times sweeter than sucrose. The level of mogrosides sweetness depends on the percentage of mogroside-V (9) in the total mixture of mogrosides. Mogrosides mixture are Generally Recognized As Safe (GRAS) by FDA and is available in the market in the form of

liquid or solid form under the trade name Purefruit® as sweetener and flavour enhancer for food products, beverages, chewing gums, baked goods, dietary supplements, powdered drinks, national bars, and chocolates

### High intensive sweeteners approved by FDA:

High intensive sweeteners that are produced from non-natural sources must undergo premarket review for approval by FDA before it can be used as food additives in foods or other applications. These are the two semi-synthetic peptides of Aspartame and Neotame, and the four synthetic Chemicals of Saccharine, Sucralose, Acesulfame Potassium and Cyclamate.

The following are the chemicals structure and properties of these Six HIS that are approved by FDA in the United States as food additives.

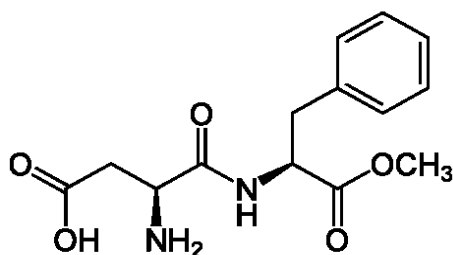
#### A. SEMI-SYNTHETIC PEPTIDES:

Both Aspartame and Neotame are manufactured by two production steps. The first step is the microbial fermentation process for separately producing the two amino acids aspartic acid and phenylalanine, the second step is the synthetic chemical process for forming the peptide bond between these two amino acids and side chains.

The non-pathogenic microorganism for the production of aspartic acid by fermentation is the bacteria *B. flavours* and the non-pathogenic microorganism for the production of phenylalanine by fermentation is the bacteria *C. glutanicum*.

In the synthetic chemical process only L- form for both amino acids are selected for forming peptide bond between the carboxylic group of L-aspartic acid and the amine group of L-phenylalanine.

#### 1. Aspartame:



**Aspartyl –phenyl alanine-1-methyl**

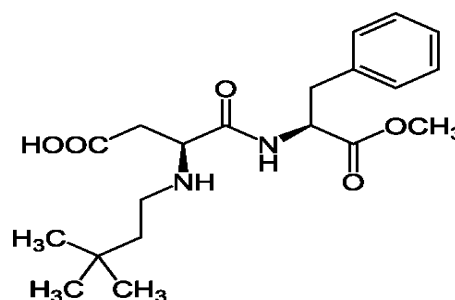
Aspartame (10) is a zero calorie with about 200 times sweeter than sucrose. It is methyl ester of the dipeptide of the two amino acids aspartic acid and phenyl alanine (11).

Aspartame is approved in 1981 for use under certain conditions as a table top sweetener, and as sweetener for a wide variety of foods, including chewing gum, candies, cold breakfast cereals, beverages, drinks, and desserts. It is not suitable for baked goods or any other products required heating during its production process or before service. This heat instability of Aspartame is due to its dipeptide structure. The heat breakdowns the dipeptide bond into the two free amino acids L-aspartic and L- phenyl alanine. Breaking down this dipeptide bond causes the loss of Aspartame sweetness property.

Aspartame is metabolized in the human digestive system into its two amino acid of phenyl alanine and-aspartic acid. People with the rare disease of disorder phenylketonuria (PKU) (12) cannot metabolize phenylalanine and should avoid aspartame in their diets. Due to this rare disease, Aspartame- containing foods and beverages must be labelled to inform individuals with PKU that the product contains phenylalanine.

Acceptable daily intake (ADI) of Aspartame is 33 mg/kg body weight and it is available in the market under brand names NutraSweet®, and equal®.

#### 2. Neotame:



**N-(N-(3, 3-dimethylbutyl)-L-α-aspartyl) 1-methyl ester**

Neotame (13) is a modified form of Aspartame, created by combining it with another chemical. This makes it more stable, sweeter and prevents it breaking down into phenylalanine during the metabolic process.

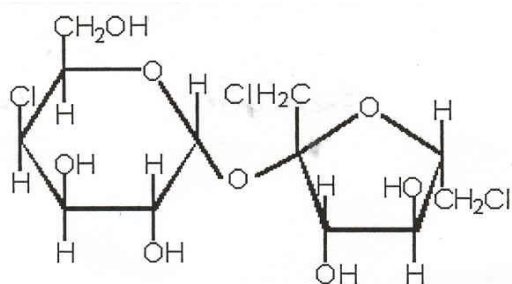
It is approved by FDA for use as sweetener and flavour enhancer in food products and beverage. It is marketed under the brand name Newtame®.

Neotame is a zero calorie sweetener with about 8,000 to 13,000 times sweeter than sucrose depends on its application and formulation. It is chemically similar to aspartame, but it is more sweeter and more stable than aspartame. Neotame stability is due to the 3, 3-dimethylbutyl group attached to the amino group of the amino acid aspartic acid.

This attached 3, 3-dimethylbutyl group to aspartic acid block peptidase enzymes in the digestive system to hydrolyze the peptide bond into the two free amino acids aspartic acid and phenyl alanine. This peptidase enzyme resistance makes Neotame safer for individuals with the rare disease of disorder phenylketonuria (PKU) and help manufacturers to eliminate the warning label that the product contains phenyl alanine (13).

Neotame is metabolized in human system into methanol and di- esterified peptide residue. The amount of methanol released in human blood stream is very low due the low level of Neotame used as sweetener in foods, beverages and other applications.

### 3. Sucralose:



#### Tri-chloro-galacto-sucrose

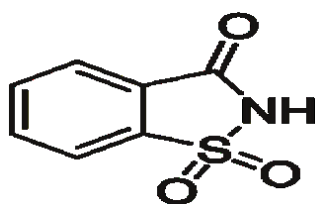
Sucralose (16) is a common name for a new high intensity sweetener derived from sucrose. It is about 600 times sweeter than sucrose and produced by the selective chlorination of sucrose.

It is safe for human consumption (17) approved by FDA (18) in United States and also approved in more than 35 countries by other similar organizations. Its acceptable daily intake (ADI) (19) is 15mg/kg body weight.

Sucralose is a non-chloric, that does not breakdown in the body into the two monosaccharides glucose and fructose and does not promote tooth decay (20). It is soluble in water and has excellent stability in wide range of PH and temperature. These properties (21) make Sucralose suitable for wide applications (22) including processed food and beverages. It is available as a tabletop sweetener under the trade name Splenda®.

## B. SYNTHETIC CHEMICALS:

### 1. Saccharin:



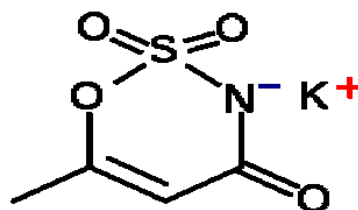
Benzoic sulfilimine

Saccharine is a zero calorie with 200 to 700 times sweeter than sucrose depend on the type of application and formulation. Saccharine was discovered in 1879 and is approved for the use in foods as non-nutritive sweetener under certain conditions, in beverages, fruit juice, soft drinks, and processed foods. It is also available as a sugar substitute for table use. Acceptable daily intake (ADI) for Saccharine is 15 mg/kg body weight and it is marketed under several brand names include Sweet in Low®, and Sweet Twin®

In the early 1970s, saccharine was linked to the development of bladder cancer in laboratory rats, which led Congress to mandate additional studies and a warning label (14) on products containing saccharine.

Human studies eliminated this bladder cancer concern and demonstrated that the harmful results on laboratory rats were not relevant to human. In the year 2000, the National Institute of Health (NIH) removed saccharine from the list of a potential carcinogens (15) and all products containing saccharine are no longer have to carry the warning label.

### 2 Acesulfame potassium:



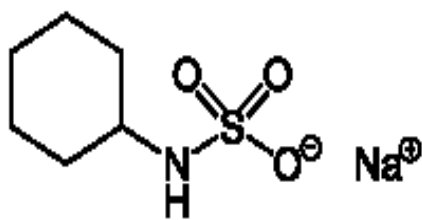
#### 6-methyl-1, 2, 3-oxathiazine-4(3H)-one 2, 2-dioxide

Acesulfame potassium (23) also, known by the name Acesulfame K or Ace K. It is non-nutritive sweetener with 200 times sweeter than sucrose but has a slight bitter after taste when added to foods or beverages at high concentration. Some researchers reported that Acesulfame K may increase the occurrence of breast cancer in laboratory animals, but FDA maintains its safety status (23).

Acesulfame K is stable under heat and under moderately acidic conditions. This stability properties making Acesulfame K suitable for baked goods, carbonated beverages, protein shake, pharmaceuticals and in any other products that required a long shelf life. Its Acceptable Daily Intake (ADI) (19) (23) is 15 mg/kg body weight and it is marketed under trade name Suncett®.



### 3. Cyclamate:



Cyclohexanesulfamic acid

Cyclamate (24) is the sodium salt of cyclamic acid. It is 30 to 50 times sweeter than sucrose and it is marketed as a table top sweetener under trade name Twin® in Canada and over 50 countries.

In 1970 Cyclamate was band from United States because laboratory experiments showed that large doses of cyclamate in a diet caused bladder cancer in rats. Recently United States lifted its band (25) after the Cancer Assessment Committee of the FDA decided that cyclamate is not carcinogenic (26). Its acceptable daily intake (ADI) (25) is 11 mg/kg body weight.

#### Conclusion

High-intensity sweeteners (HIS) are non-nutritive ingredients used to sweeten and enhance the flavor of foods and are commonly used as sugar substitutes or sugar alternatives (26) and like all other ingredients added to foods, beverages and other products it must be safe for consumption.

High intensive sweeteners (HIS) from natural sources are refer to natural sweeteners and considered to be safe with GRAS status. The two natural sweeteners Rebaudioside-A extracted from Stevia leaves and Mogrosides extracted from Luo Han Guo (Monck fruit) were considered to be safe with GRAS status in the year 2008 and 2010 respectively.

Semi-synthetic peptides such as Aspartame and Neotame and synthetic chemicals such as Saccharine Sucralose, Acesulfame potassium, and Cyclamate, are not natural and refer to artificial sweeteners.

These artificial sweeteners before being approved must undergo extensive safety evaluation in tests with humans and animals and must meet the same standard of safety for consumption by consumers including pregnant women and children. In United States, these artificial sweeteners were approved by FDA as safe for applications as food additive sweeteners in foods, beverages and pharmaceuticals.

Because high-intensity sweeteners are many times sweeter than table sugar (sucrose), smaller amounts of high-intensity sweeteners are needed to achieve the same level of sweetness as sugar in foods.

Plus the availability of a variety of low-calorie sweeteners (27) for use in foods expands the capability to develop reduced-calorie products that better meet consumer needs and desires. In addition, blending some low-calorie sweeteners in foods and beverages may also act synergistically to produce the desired level of sweetness with smaller amounts of each sweetener and resulting taste often better meets consumer expectations of a sweetness profile close to that of sugar.

People may choose to use high-intensity sweeteners (HIS) in place to sugars for a number of reasons (28), including to these HIS do not contribute calories or only contribute a few calories to the diet.

High Intensive sweeteners ,assist people in losing weight, avoiding obesity diseases and other health associated with high caloric intake by replacing common sugars such as sucrose, dextrose, high fructose corn syrup and corn syrup in foods and beverages with these non-nutritive, zero calorie high intensive sweeteners without changing people's diet habits and taste.

Assist diabetics to control their blood sugar levels without scarifying their regular diets and taste. Also, Patients with reactive hypoglycaemia (29) producing excess insulin (30) after the break down of complex carbohydrates or sucrose in their diets into glucose that is released into the blood stream and quickly metabolized causing blood glucose levels to fall below the proper level for the body and brain function. As a result, these patients like diabetes, must avoid consuming foods containing high-glycaemic index ingredients (30) such as complex carbohydrates or sucrose and must choose foods containing sugars substitutes such as the high intensive sweeteners as alternative.

There are other several advantages for the application of high intensive sweetener in foods, beverages, candies, chewing gums and other products. For example, these High intensive sweeteners are non-fermentable by oral microflora. This non fermentable property helps consumers to prevent dental plaque and decay.

Other examples that benefits both consumer and manufacturers are the wide range stability of pH and temperature for these high intensive sweeteners that allows its applications in products required long shelf life at room temperature.

Consumers' concern for weight management is the major market demand for these zero calorie high intensity sweeteners as a replacement for sugars in their diets and the worldwide consumption of these low calorie high-intensity sweeteners is largely

dependent on the production of diet carbonated soft drinks and low-calorie foods. Beverages market are the largest end-use for these high-intensity sweeteners, followed by foods, tabletop sweeteners, personal care products (such as toothpaste), and pharmaceuticals.

The World Health Organization estimates that there are over a billion people globally who are overweight and over 400 million of which are obese. Unfortunately, these numbers are expected to continue increasing and the market demand for these zero calorie, non-nutritive High intensive sweeteners (HIS) will increase. It is estimated that the global market of high intensive sweeteners for the year 2014 was 9.4 billion and it is expected to reach 9.9 billion by the year 2016. The old discovery Saccharine is the only high intensive sweeteners that is facing tough competition from the newly discovered competitors and its market demand continue declining.

Despite these zero calorie high intensity sweeteners are approved by FDA in United States and by similar organization in other countries and are recommended by physician or registered dietitian for a large segments of the population for several health reasons, some people continue to question the safety of these low calorie high intensity sweeteners in their diets.

In United States, FDA continues to maintain and review scientific literatures on the safety of these approved high intensive sweeteners in foods, beverages and other products.

In the case of new evidence suggested that a product containing the approved low calorie high intensity sweetener is unsafe, FDA is responsible to review such suggestion and take the proper action. Even, these extensive safety evaluations by FDA and by other similar organizations worldwide it did not change the safety concern of some people worldwide.

**Conflict of interests:** We declare that we have no conflict of interests.

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## The impact of Quercetin like flavonoid antioxidants on Cancer Therapy

Zafer Akan<sup>1\*</sup>

### Abstract

Uncontrolled consumption of medical plants may lead controversial result over the patients who are receiving radiotherapy or chemotherapy for cancer treatment. Especially, flavonoid free radical scavenger including chemical and plants may not be innocent as much as thought. Free radical scavenger antioxidant extracts uses for commonly for two aims; the prevention of cancer and therapy of cancer.

In the light of recent developments the impact of antioxidant usage on cancer treatment and prevention is shortly reviewed in this article

**Keywords:** Antioxidant, Cancer, Oxidant, Therapy, Prevention

Human body has a critical balance between the oxidant and antioxidant status. Oxidants called Reactive oxygen species (ROS) and Reactive Nitrogen species (NOS) are highly active chemical molecules which are generated predominantly during cellular respiration and normal metabolism called endogenous Oxidants.

Other kind of oxidants are exogenous specifically produced by the ionizing radiation are highly toxic chemicals.

These products can damage many biological macro molecules; they are capable of changing enzyme functions, damage DNA materials and lipid peroxidations through the all cell membrane (1). Thus, they are evaluated as carcinogenic.

The superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX) antioxidant enzyme protein binds to metals and minerals and inhibit production of free radicals

Moreover some antioxidants such as glutathione enzyme, albumin, vitamins C and E, carotenoids, and flavonoid capture the free radicals and inhibits oxidation activities, and they may prevent oxidative chain reactions.

Other important group of antioxidants such as lipases, proteases, DNA repair enzymes, transferases, and methionine-sulfoxide reductases are responsible for repair process of damaged DNA by the superoxides.

In other aspects, due to the DNA damaging effect, radiation caused by the reactive oxygen species are key components to destroy cancer cells during radiotherapy.

As it might be expected, the reducing environment inside the cell helps to prevent free radical mediated damages.

This reducing environment is maintained by the action of antioxidant enzymes and substances, such as superoxide dismutase (SOD), catalase, glutathione peroxidase, glutathione, vitamins C and E (2).

If the balance is disrupted and if ROS is produced excessively, over ROS may lead to starting of programmed cell deaths and may accelerate the process of aging (3).

In normal conditions, herbal sourced antioxidant intakes could be beneficial for cancer prevention (4, 5), coronary artery disease prevention (6) and slowing down the aging process.

But what will happen if the cancer patient takes artificial herbal sourced antioxidants, especially the free radical scavenger flavonoids which are abundantly present in many herbs, fruits and grains during therapy. Will it be helpful to the cancer therapy?

Some studies have shown that NAC and Trolox increases the activation of the small guanosine triphosphatase (GTPase) RHOA, and blocking downstream RHOA signalling abolished antioxidant-induced migration. These results demonstrate that antioxidants and the glutathione system play a previously unappreciated role in malignant melanoma progression. (7)

It is possible that the supplements did not trigger cancer, but rather accelerated the progression of existing diagnosed and undiagnosed cancers, making later discovery of the disease likely.

In other words, it "could be that while antioxidants might prevent cancer therapy targeted DNA damage in cancer cells too and thus impede tumor initiation once a tumor is established, or antioxidants might facilitate the malignant behaviour of cancer cells.

Some other findings imply that eliminating antioxidant enzyme activity may be an effective strategy to enhance susceptibility to cell death in cancer cells that may otherwise survive the ECM-detachment (8)

Most recent findings strongly suggest that reducing environment is beneficial for all cells survival not just normal/non-cancer cells.

Beside the in vitro studies, some clinical trials are also providing evidence on the relation between cancer and antioxidants.

For example, Physicians' Health Study II (PHS II): This trial examined whether supplementation with vitamin E, vitamin C, or both would reduce the incidence of cancer in male U.S. physicians ages 50 years and older. The results, reported in 2009, showed that the use of these supplements (400 IU vitamin E every other day, 500 mg vitamin C every day, or a combination of the two) for a median of 7.6 years did not reduce the incidence of prostate cancer or other cancers, including lymphoma, leukaemia, melanoma, and cancers of the lung, bladder, pancreas, and colon and rectum (9).

A lot of randomized controlled clinical trials also did not provide evidence that dietary antioxidant supplements are beneficial in primary cancer prevention (10).

The literature has a lot of controversial and immature datas about the question of is antioxidants beneficial or not?

For example curcumin has antioxidant properties, for this reason effect of curcumin on prostate cancer treatment has been studied by the Hejazi et al.

The result implies that Curcumin is an antioxidant agent with both radiosensitizing and radioprotective properties but no significant outcome was observed regarding to treatment outcomes over the prostate cancer patient (11).

However other important antioxidant vitamin E ( $\alpha$ -tocopherol) is suggesting as strong therapeutic against cancer prevention and therapy (12).

## Conclusion

Antioxidants do not act selectively, both endogen and exogen may prevent not only healthy cells and DNA, but also may prevent cancer therapy targeted DNA damage in cancer cells too.

Strong immune system may take over cancer, to protect ROS balance, not just a for reducing cancerous environment but also is necessity to protect life.

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## Associations between nutritional composition and farming type of organically and conventionally grown cereals

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### Abstract

**Objective:** To determine the nutritional composition including the health beneficial dietary component  $\beta$ -glucan of different cereals grown by organic and conventional farming, and to find out the influence of the cereal kind and farming method on their values, as well as the possible associations between particular nutritive components in cereal samples and farming type.

**Material and Methods:** 27 different cereal samples grown at three locations were analysed by standard AOAC methods of analysis for their nutritional composition. A mixed-linkage  $\beta$ -glucan assay kit (Megazyme Ireland) was used for determination of the health benefit dietary component  $\beta$ -glucan value. Cereal kind-farming method by chemical-technological trait bi-plot analysis was done within R 2.9.0 program environment for investigation of associations between average value of cereal nutrients and farming type.

**Results:** A significant increase in the content of ash, dry matter, protein and fat in organically produced cereals was noticed in comparison with those which were produced either by conventional or in conversion method. Cereal kind-farming method by chemical-technological trait bi-plot revealed existence of positive and negative associations between the average value of particular cereal nutrient and farming type.

**Conclusion:** Based on the cereal kind-farming method by chemical-technological trait bi-plot the possibilities are derived that could be used for agronomic practice, breeding and food processing industry at improving the important properties-dry matter, protein, fat, ash, moisture and  $\beta$ -D-glucan in cereal crops. Organic farming method proved to be effective for oat for the all examined chemical-technological traits except moisture and ash, and for barley for dry matter, beta-glucan, ash and protein contents.

**Keywords:** cereals, organic farming, conventional farming, nutrition,  $\beta$ -glucan, associations

### Introduction

Food is essential to life and wellbeing of the population. A food system operates on the basis of the following stages: growing, harvesting, processing, packaging, transporting, marketing, consumption, and disposal of food and food-related items. Food systems are either conventional or alternative according to their model of food lifespan from origin to plate (1).

According to the EU platform for an action on diet, physical activity and health, changes in diet must be done because recent decades have been seen a trend towards less sustainable and less healthy diets, with European citizens consuming too much energy, too many calories, too much fat and sugar, and salt. As a consequence wide-spread diet-related diseases are: obesity, type 2 diabetes, hypertension, osteoarthritis, and cancer. Many studies have proved that cereals are naturally rich with health benefit components such as dietary fibre components (2).

There is evidence that the soluble dietary compound (1 $\rightarrow$ 3)-(1 $\rightarrow$ 4)- $\beta$ -D-glucan has health claim related to cereal-derived  $\beta$ -glucan that may significantly reduce the risk of diseases and strengthen the immune system (3-10).

Organic food systems in comparison with the conventional ones, are characterized by a reduced dependence on chemical inputs and an increased concern for transparency and information (11, 12). Principles of organic food production are: biodiversity, ecological balance, sustainability, natural plant fertilization, natural pest management, and soil integrity. Organic food products are grown or raised by a producer who uses practices in balance with the natural environment, using methods and materials that minimize negative impact on the environment. They are produced on land that has been free of known and

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perceived toxic and persistent chemical pesticides and fertilizers for at least three years prior to certification,

and synthetic fertilizers and pesticides are not used in production. Organic foods are planted on a rotating basis within the farm system. Crops are rotated from field to field, rather than growing the same crop in the same place year after year. Cover crops such as clover are planted to add nutrients to the soil and prevent weeds. Organic meat, poultry and egg products come from farms that use organic feed, do not administer added hormones to promote growth or any antibiotics and they allow animals the space and freedom to behave naturally.

In 1992 the European Community developed organic standards and a certification scheme (13). The International Federation of Organic Agriculture Movements (IFOAM) also has a set of organic principles which were the basis of the guidelines for organically produced foods of the internationally recognized Codex Alimentarius (14) of the World Health Organization and Food and Agriculture Organization of the United Nations (WHO/FAO food standards). Codex Alimentarius is the internationally accepted food safety standard for all food products traded worldwide. There is a set of standards within the Codex Alimentarius that covers organic food.

In October 2002, the production and marketing of organic food came under regulation by the US Department of Agriculture's (USDA) National Organic Program. The National Organic Standards Board, a federal advisory panel to the USDA for developing organic legislation.

The law for organic agricultural production, food products and food in Republic of Macedonia was introduced in 2009, and the changes and supplements in 2011 (15).

## Material and Methods

The content of nutritive components (moisture, ash, dry matter, crude protein and crude fat) in 27 different cereal samples: wheat, rye, barley, oat, and millet, grown at three locations during 2013 was analysed by standard AOAC methods of analysis.

### Determination the content of $\beta$ -glucan

A mixed-linkage  $\beta$ -glucan assay kit (Megazyme Ireland) was used for determination in the analysis of the health benefit dietary component  $\beta$ -glucan value, based on the method published by McCleary and Codd 1991 (16). The method has been accepted by the AOAC (Method 995.16), AACC (Method 32-23.01) and ICC Standard Method (No.166).

The principle of the method in brief is that cereal samples (1 g in duplicate) were suspended and hydrated in sodium phosphate buffer pH 6.5 for hydrolysis with highly purified lichenase enzyme and filtered, than hydrolysis with  $\beta$ -D-glucosidase.  $\beta$ -D-glucan is specifically hydrolysed by lichenase to

oligosaccharides, which are quantitatively cleaved to glucose by  $\beta$ -glucosidase. Glucose is measured using glucose oxidase - peroxides - buffer mixture.

The results have been shown as a mean values  $\pm$  standard deviation. The value of  $\beta$  content was calculated on dry weight basis.

### Cereal kind-farming method by chemical-technological trait bi-plot analysis

In order to find out the existence of associations between average value of cereal nutrients and farming type, cereal kind-farming method by chemical-technological trait bi-plot analysis was done within R 2.9.0 program environment (17).

### Statistical analysis

Data were tested for significance using analysis of variance, the F-test using the software package Statgraph 3.0 (Statistical Graphics, Warrenton, Virginia, USA).

## Results

### Determination the content of cereal nutrients

The results obtained from the investigations on the content of cereal nutrients: ash, protein, fat and dry matter are presented in the Figures 1-8.

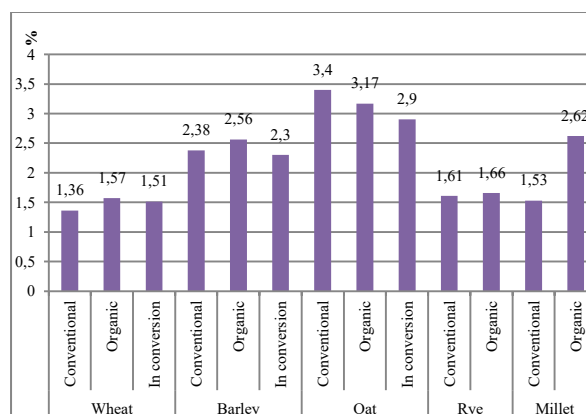


Figure 1. Content of ash in cereal samples cultivated conventionally and organically

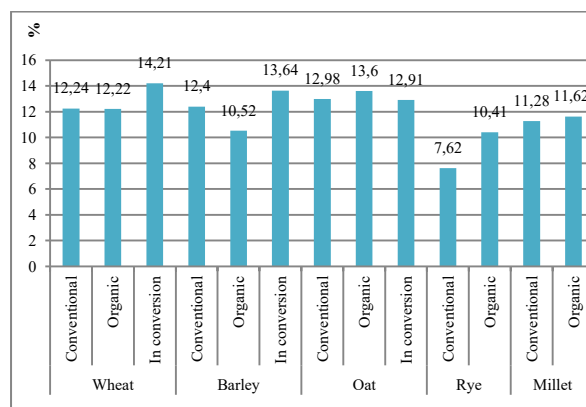


Figure 2. Content of protein in cereal samples cultivated conventionally and organically



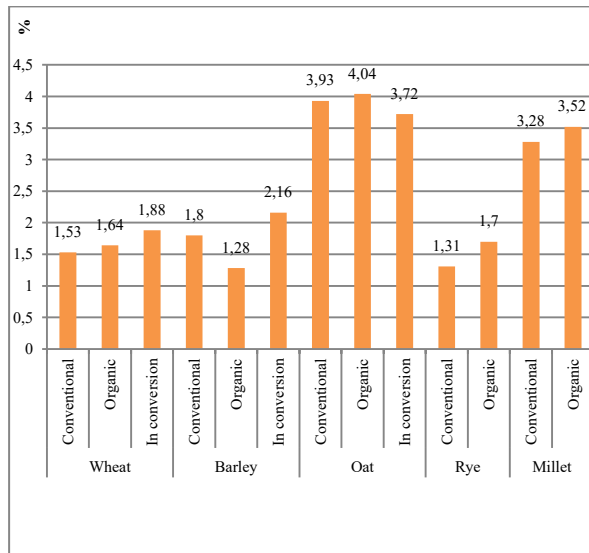


Figure 3. Content of fat in cereal samples cultivated conventionally and organically

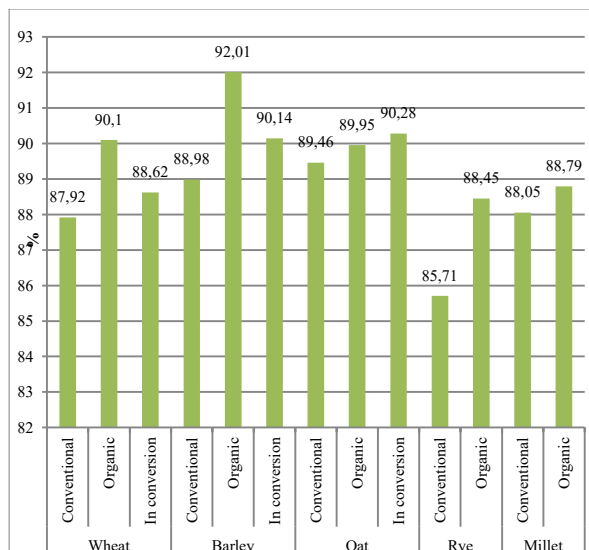


Figure 4. Content of dry matter in cereal samples cultivated conventionally and organically

From the Figures (1-4) can be seen that there was a significant increase in the content of ash, dry matter, protein and fat in organically produced cereals in comparison with those which were produced either by conventional or in conversion method: the increase of ash content was 15% with wheat, 7% with barley, and 71% with millet, the increase of protein content was 37% with oat and 3% with rye, and the decrease of 15% with barley, and the increase of crude fat content was 15% with wheat, 3% with oat, 29% with rye and 7% with millet.

**Determination the content of  $\beta$ -glucan content in cereal samples**

The results obtained from the investigations on  $\beta$ -glucan content in cereal samples are presented in Figures 5.

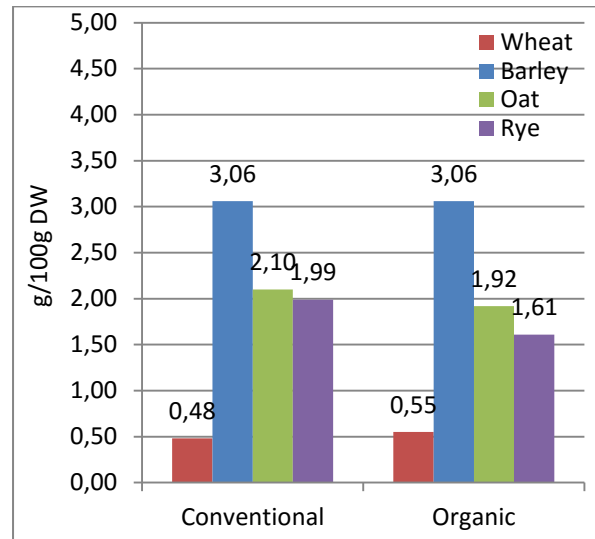


Figure 5. Content of  $\beta$ -glucan in wheat, Barley, oat and rye cultivated conventionally and organically.

Comparing the values of  $\beta$ -D-glucan in organic and conventional cereals (Figs. 5-8), it was noticed the following: slight increase in organic wheat (9.84%), and slight decrease in oat (2.91%), and small decrease in rye (18.06%).

**Associations between average value of nutrients and cereal farming type**

Figure 6 Re-present the associations between average value of nutrients: ash, dry matter, crud protein, crud fat and  $\beta$ -glucan in cereals investigated, and the farming type.

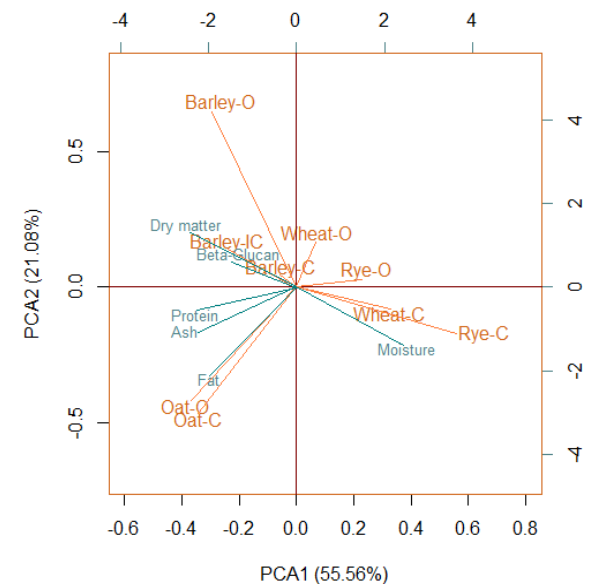


Figure 6. Cereal kind-farming method by chemical-technological trait bi-plot. (dry matter, protein, ash, fat, moisture,  $\beta$ -glucan)

Cereal kind-farming method by chemical-technological trait bi-plot (Figure 6) revealed existence of negative associations between: average dry matter content and average beta-glucan content

and wheat and rye conventionally farmed; average fat content and wheat and rye organically farmed and to lesser extent for wheat and rye obtained from conventional farming method; average protein content and average ash content and wheat and rye produced with the conventional farming method; average moisture content and barley produced with the in conversion farming method and little weaker for barley obtained from conventional farming method.

## Discussion

Our research has revealed that barley grown by either conventional or in conversion farming method proved to have the highest content of dry matter. Oat obtained from organic farming method exhibited the highest fat, protein and ash content. In comparison of the organic to conventional farming method, there was no change in the content of  $\beta$ -D-glucan value for barley which was grown either by organic or conventional farming.

Cereal kind-farming method by chemical-technological trait bi-plot explained high proportion of G + GE variance of 76.64% and revealed existence of positive associations between: average dry matter content and average beta-glucan content and barley produced from the in conversion farming method and also little weaker for barley produced with the conventional farming method; average fat content, average protein content and average ash content and oat produced with the organic farming method and also little weaker for oat produced with the conventional farming method; average moisture content and wheat and rye conventionally farmed.

A phenotype by trait bi-plot can help understand the associations among breeding objectives and identify traits that are positively or negatively correlated, traits that are redundantly measured, and traits that can be used in indirect selection for another trait (18). It also helps to visualize the trait profiles of phenotypes (19), what is of particular importance for selection programs, agronomic practice and food processing industry.

## Conclusion

Based on the cereal kind-farming method by chemical-technological trait bi-plot the possibilities are derived that could be used for agronomic practice, breeding and food processing industry at improving the important properties-dry matter, protein, fat, ash, moisture and  $\beta$ -D-glucan in cereal crops.

As contents of protein, dry matter,  $\beta$ -D-glucan, fat and ash were positively associated the same-directional breeding for these traits would be possible, while due to negative association with moisture the co-breeding for moisture content in the same direction would not be possible.

Barley grown by either conventional or in conversion farming method proved to have the highest content of dry matter and  $\beta$ -D-glucan content when compared to

other cereals investigated, whereas oat obtained from organic farming method exhibited the highest fat, protein and ash content.

Organic farming method proved to be effective for oat for the all examined chemical–technological traits except moisture and ash, and for barley for dry matter, beta-glucan, ash and protein contents. Average ash content and average moisture content were positively associated leading for the possibility of the same-directional breeding for these traits.

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**Conflict of Interest:** The authors declare that there are no conflicts of interest.

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