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Safety of additives in food for human health

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Abstract
Food additives give food and cosmetics a longer shelf life, allowing manufacturers to have higher income. Additives are also used to preserve flavor and color. For centuries people used salts, vinegar, herbs, boiling and cooling to preserve food naturally, but in the last 50 years, artificial preservatives have become a common method.
While some food additives and preservatives provide nutritional benefits or improve food safety, others - from colors and flavors to thickeners and bleaches - are added to attract consumers and have known or potential health risks.
It's not unusual for a food additive that was believed to be safe for consumers to see later that it's toxic. Some studies have shown that additives can cause headaches, nausea, weakness and difficulty breathing. New research has shown that the combination of additives and certain foods can harm human nerve cells. The truth is that we do not understand all the long-term effects that additives can cause on human health, because artificial additives are a relatively new invention.
For now, consumers should choose what kind of food they will buy. Additives will not be banned until enough evidence based on research is collected to determine the exact effects they have on the human organism.

Keywords: food additives, food safety, human health

1. Introduction
Authorities (The US Food and Drug Administration (FDA), EFSA at the European Union level, etc.) have published lists of hundreds of approved additives, but there are still several clinical studies to prove if some of them are safe for human consumption, that is, do they cause adverse reactions in some people, especially those who are sensitive to additives (which is only a small percentage of the population). The studies that exist are often unsuitable to assess the degree of risk. It has also been reported that problems often arise when additives are taken at high doses, which can be very harmful to the human body. Despite this, people still claim that all additives are harmful. Often, you can look at the food packaging and identify artificial ingredients, preservatives or a long name that does not sound like food. But although they can spot and know that they are not a healthy option, most people do not bother to look for these "ingredients". In our culture, with easy access to food, it is easy to ignore the fact that most of the products we buy in traditional supermarkets are processed and contain additives.

1.1. Known or potential health risks
Food additives and preservatives are associated with the following, primarily animal studies:
- Cancer of laboratory animals such as rodents,
- Asthma and allergic reactions related to chemicals such as sulphites and nitrites and nitrates that prevent color change in the meat and are considered to be one of the worst food additives,
- Symptoms, such as nausea and diarrhea, which may be part of an allergic reaction,
- Pre-term delivery related to artificial sweeteners, according to the Danish study in 2010 and the Norwegian study in 2012,
- Hyperactivity and attention deficit in children,
- Resistance to antibiotics in humans due to their use in animal feed,
- Headaches of substances such as monosodium glutamate (MSG),
- Increased risk of heart disease from the accumulation of phosphate in the body in those at risk,
- Risk of weight gain from added sugars and sweeteners, hormones or substances that impede hormonal regulation,
- Neurological problems, such as those in the consumption of aspartame in rats.
- The real danger of food additives and preservatives, natural or synthetic, is that no one knows what the real collective hazards are [1].

2. Materials and methods
The methodological procedure includes a basic component, a research of domestic and foreign literature in the field of contemporary trends in the use of food additives in human nutrition and other professional literature in order to provide information to consumers on the safety and impact of food additives on human health. Case studies from practice are used, determined on the basis of the allegations given in the relevant literature. This allowed parallel consideration, with

comparative views on the aspects of the safety and impact of food additives on human health, presented through various practices, examples in the literature, as well as applied laws, which led to conclusions about the possibilities for further development.

The following scientific methods were used in appropriate combinations: inductive and deductive method, method of analysis and synthesis, abstraction and concretization method, generalization and specialization method, method of proof, comparative method, compilation method and empirical method.

3. Results and discussion

3.1 What are food additives

The adjective "food" indicates that additives are used exclusively in food production, in contrast to other additives used in the production of plastic masses, cosmetics, washing and cleaning agents, lubricants for the automotive industry, etc.

Food additives are substances with known chemical composition, which are not consumed as food, nor they are typical food ingredients, regardless of the nutritional value, and they are added to food to improve the technological performance and maintain the sensory properties.

Additives are added to food in the production process, during preparation, processing, shaping, packaging, transport and storage. Modern food production can't be imagined without the addition of additives, under precisely determined conditions and with a well-established cause. The quantities used to achieve the technological effect are measured in milligrams, and only a few additives are added to the food in grams [2].

Additives that after their addition have reached their technological or sensory effect and have not degraded become one of the constituents of that food.

Additives and their mixtures can be added to food under the following conditions: to be toxicologically evaluated, their use is technologically justified, unless the final effect can't be achieved in ways that are economically and technologically more applicable, to be added to food in quantities permitted by special regulations, by adding them consumer should not be misled for the true nature, ingredients or nutritional value of food, do not significantly affect the natural taste and smell of the food in which they are added, if this is not a special purpose, by mixing and adding to the food, are not generated toxic substances (products) during processing, storage and use.

The use of additives is directly related to their basic functional, technological properties, so today they are divided into 26 categories: colors, preservatives, antioxidants, emulsifiers, stabilizers, thickeners, gelling agents, acidity regulators, acids, clotting, flavor enhancers, sweetening substances (sweeteners), modified starches, polishing substances, moisture retaining agents, flour treatment substances, hardeners, volumetric enhancers clever, compressive gases, emulsifier salts, anti-foaming agents, coagulants, carriers, foaming agents, packaging gases and sequestrants.

The lists of food additives, the manner of use, the quantities that are allowed for addition in food, are set out in a series of fundamental regulations [3].

3.2 Labeling of the additives

Additives are labeled with E-number, as a confirmation of the toxicological evaluation and classification of a particular additive.

Substances similar to additives, which also have a technological role in production, do not have an E-number and are otherwise labeled (aromas and enzymes), while the auxiliary substances in the production process, because of the way of action that differs from the action of the actual additives in production of food, should not be labeled, although some of them have an E-number.

When added to food, additives to the product declaration must be labeled with the name of the category, which is the technological purpose of the use of additives, followed by their specific chemical name or E-number. If the additive has more than one technological function in the production of some food, it is necessary to state the technological effect of which additive has been added to the food, which in this case becomes the category of the additive. The primary functional or technological characteristic does not exclude the possibility that certain additives may have some other functional properties if the concentration or amount of the additive added to the food is changed. Also, other functional actions do not exclude the effect on food at the same time as the additive is added due to the underlying functional action.

A thin red line between the need and the justification for the use of additives is not always clearly drawn, because when health is not compromised, then technological necessity in most cases is the work of food producers and is not a reason to ban the use of additives in some foods. With the increasing number of new products, with competition on the market, food producers sometimes use additives not only because of technological needs, but also because of differences, offer, earnings, which is exactly the opposite of the basic principles for the use of food additives. In order to be able to market and retain some time on the market, biological, organic food processed for the market allows the use of some additives. It only speaks of the fact that avoiding the use of food additives is neither an objective nor a need for producers who respect the prescribed need for the use of additives [4].

3.3 Toxicological evaluation of additives

When some substance should be count in nutritional additives, it is necessary to produce a specification of the technical data. The technical specification on the data must cover:

1. Identity of a substance that encompasses the chemical name and precise chemical structure;
2. Physio-chemical properties of pure substances;
3. Microbiological criteria for pure substance;
4. A brief description of the technological synthesis process or method of obtaining;
5. Specificity of indications of the microorganism type, if a microbiological method for obtaining a composition is present;
6. The specificity of indications of a genetically modified organism, if such a method of obtaining is present;
7. Methods for analysis of pure substance, as well as the method of analysis in food;

8. Reactivity and stability in food;
9. Required quantities and recommendations for use;
10. Dissatisfaction or diversity of acting in the technology of food production.

Food additives prior to use in food production must be toxicologically tested and evaluated. Toxicological studies include acute, subacute, and chronic toxicity and carcinogenicity, and the detailed toxicological research protocol includes:

1. General requirements for toxicological evaluation of additives;
2. Protocol for conducting research (study);
3. Toxicological procedure in the order:
    a. Fundamental Studies: metabolism/toxicokinetics, subchronic toxicity, genotoxicity, chronic toxicity and carcinogenicity, toxicity in reproduction and development.
    b. Other studies: immunotoxicity, allergenicity, intolerance, neurotoxicity, research on people (volunteers), in vitro studies as an alternative to in vivo study, special studies, Acute toxicity, sensitivity and irritation of the skin and eyes.
4. Literature data;
5. Summary of results and conclusion.

With multigenerational studies are followed the reproductive and developmental course, with the metabolic and pharmacokinetic studies the impact after resorption, the time of excretion, while with special techniques in genetic studies, changes on the cellular level are observed. The interaction of additives with other ingredients in food and medicine is also examined. After thorough research, the highest amount of additives in which no toxicological effects on health or "No observed adverse effect level" (NOAEL) have been observed. If several studies show different but similar results, the lowest value for determining NOAEL is taken. The minimum amount of a compound, and also an additive that can negatively affect human health, is "Lowest observed adverse effect level" (LOAEL). For each additive for which the largest amount of no toxicological effects on health (NOAEL) has been separately determined, it is usually divided with the safety factor 100, taking into account possible differences in extrapolation with respect to individual parts of the population, with particular attention to the population of children and the elderly as risk groups. Since the difference between NOAEL and LOAEL is insignificant, both the one and the other value can be taken into account for the calculation.

This risk assessment takes into account the amount of additives that would perform the technological role in food production to be respectable, which means that potential additives that have low NOAEL, usually after the risk assessment can't be listed, because the quantities are too small for the purpose for which they are intended.

After previous research and calculations using a security factor, the values obtained serve as the basis for determining an "Acceptable Daily Intake" (ADI) [5].

Thus, in 1957 the first list of all food colors used for staining food in different countries of the world was made. There are 135 different colors that are used by different countries. Of these colors, only 22 are allowed today, while 113 are forbidden for use in food. Today's list contains 42 food colors, four of which can be used only for surface decoration and must not be eaten.

In the 1960s, lists of additives were established, and contrary to the established opinion, the number of additives used today is not much larger than 30-40 years ago. Only a few new ones are added to the list of allowed additives, while several additives are forbidden for use in humans [6].

3.4 Acceptable Daily Intake (ADI)

"Acceptable Daily Intake" (ADI), which is defined as the amount of additives as an integral part of the food that can be consumed daily throughout the entire lifespan without any risk to health. The acceptable daily intake for each additive individually is expressed in mg/kg of body weight. Based on determining the intake of foods consumed daily and the amount of additives in that food, the actual daily intake for each additive can be determined and evaluated whether they exceed the acceptable daily intake for each individual additive. Like all other research and conclusions related to human health, additives and their established ADI remain under surveillance in order to be revised at the moment of new knowledge or better analytical methods.

The assessment ADI is "not established", it is a non-numerical assessment of safety of additives that have not reported a health problem with available toxicological, clinical and biochemical research, although the amount of food additives was sufficient to implement the technological requirements. In the same assessment, the input from all sources, which includes natural sources of additives, is also calculated, but also carried over from other foods.

However, if for each additive ADI is not specified, this doesn't mean that this additive can be added to the production of almost any food and in unlimited quantities. In that case, the basic principles for the addition of additives in certain foods must be applied [7].

3.5 Institutions responsible for additives

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) is an international scientific commission of experts from the FAO/WHO of the United Nations, which began work in 1955. To date, more than 1500 chemical compounds have been evaluated. The Commission makes suggestions to Member States to incorporate scientific opinions on certain additives in their legislation. Opinions contain toxicological evaluation, ADI, proposal quantities and type of food in which they may be used, as well as data according to which the health correctness of the additives will be determined.

The Directorate General for Health and Consumers (DG SANCO) is the body of the EU responsible for drafting food law, food safety and consumer rights, while scientific risk assessment of additives is carried out by The Panel Food Additives and nutrition sources added to Food (ANS) of the European Food Safety Authority (EFSA), which under that name, was established on July 10, 2008. Previously, since the founding of EFSA, it worked under another name (AFC-Panel on Additives, Flavourings, processing aids and materials in Contact with food). The basic directive on additives was

issued in 1989.

3.6 Contaminants that follow the production of pure additives

Any production of chemical compounds from natural raw materials, as well as chemical synthesis from other compounds, carries with it a possible remnant of inorganic or organic unwanted contaminants. The established health and quality parameters can be divided into general and specific. The general parameters of health correctness are the same for most compounds (e.g. metals and metalloids). Specific contaminants occur in the process of chemical synthesis of certain compounds as a residue from the starting compound, the extraction solvents used, so that other compounds are formed, often similar to the basic additive. Additionally, the expected purity or concentration of additives in the final product, "pure additive", is determined by several conditions and can vary from additive to additive, but always is determined the highest possible purity that can be achieved with a certain technology, with the slightest contamination as a result of production [8].

3.7 Additives whose addition to food is limited

The daily intake (ADI) of one additive is just as important as the permission to use that additive in certain foods. In addition, it must not be contrary to the basic principles that allow the use of food additives, and the daily intake is a reflection of the permissible amounts of a particular additive to carry out the technological function, food habits and risk assessment.

Although there is a very high level of compliance, there are differences, as well as some doubts that are not emphasized anywhere. Thus, the strong acids and bases do not have a specific ADI, because it is understood that they are used only for neutralization, so it can create an impression that they are not acutely dangerous. Form ADI of a particular additive depends the risk assessment, therefore it is necessary to comply at the level of all countries in the world [9].

3.8 Research related to certain additives

Additive addition studies, other than ADI or acceptable daily intake, take into account the highest allowed technological quantities (NDTK) that must not be exceeded in food production. Usually the amount of addition of a separate additive is much lower than NDTK. NDTK means that for each additive there is a limitation, whether it is related to an ADI overdraft or the increased addition of a separate additive would be contrary to the basic, general requirements and conditions prescribed for adding food additives.

Some additives can be added (quantum satis) in certain foods in quantities that are not specified or numerically restricted by regulations. Although there are no regulated quantities, however, these additives must not be used contrary to good manufacturing practice more than is technologically necessary or to be added to a particular food if such addition reduces the quality of food.

Studies that determine the daily intake of additives are based on a Tier approach. Tier 1 is carried out by calculating the daily intake of additives according to theoretical data on daily intake of food for a certain adult population and with the highest regulations for certain amounts of additives that are allowed in each particular food. In this way, particular types of foods and additives that are theoretically considered to be suspicious in terms of overcoming ADI are highlighted, the intake of a particular additive or circle of research is reduced to certain additives or foods, but also to parts of the population according to age.

Tier 2 bases research on the assessment of the additive intake on national data of the daily intake of certain types of food according to the age of population per year and the maximum allowable amounts of additives prescribed for each particular food. In addition, the choice of additives and foods is the result of Tier 1 research.

Tier is a relatively good appraisal input, which for certain types of foods suspected in Tier 2, based on national data on food intake, analyzes the actual amounts of additives in such foods and calculates the daily intake of additives.

Such a way of pyramidal study of the daily intake of additives is necessary due to the breadth of the research, as well as the cost of that research. But the main assumption is the unification of the research, the results to be reliable for each country individually, and the possibility of comparison because of the unification of the procedure.

The first big more detailed research on the intake of additives in the EU, involving 10 EU countries and Norway, determined that the input of most additives is under ADI. The basic objection to the research was the unequal methodology of research, data collection, and the daily intake of certain types of food. However, it has been established that the intake of some additives should be more subtly tested and refers to the preservatives (based on sulfur, benzoate and nitrite), emulsifiers (polysorbates and steroil lactylates, sorbitan monolaurates, monooleates), anti-clotting substances based on aluminum, phosphor-based acidity regulators and sweetener acesulfame K (especially for small children). Especially because of the uncertainty of the results presented, it has been agreed that the same study will be repeated after three years, but this has not happened.

Similar, but uniform and detailed research, with multiple consumer target groups, was conducted in Japan in 2000. It has been established that the intake of most additives is with a lower ADI than the nitrates whose intake exceeds ADI. It was found that nitrate sources were not the added additives, but the vegetables as a result of intensive cultivation.

The Norwegian Science Commission for Food Safety has explored the intake of sweeteners into beverages in which sugar has been replaced and concluded that the intake of acesulfame K is very close to ADI in the diet of young children, not counting the input from other sources. Since such drinks are often conserved, for small children up to 4 years the intake of the preservative benzoate exceeds the permissible ADI. This is important information, because in the daily intake the conversion of benzyl derivatives from the aromas that metabolize in the body to benzoic acid in the body, or the intake of benzoic acid from cosmetic products and syrup drugs are not calculated.

Scientific institute of Bologna "Cancer Research Center of the European Foundation of Oncology and Environmental Sciences B. Ramazzini" published a study on the aspartame sweetener in 2005 and 2006, stating that aspartame is a

multipotential carcinogen substance that causes malignant tumors in animals, leukemia/lymphoma, particularly in rat females, urinary tract cancer, and at peripheral nerves [10].

EFSA rejected the same research, arguably contradicting the research protocol, the incidence of cancer, with the fact that the quantities of aspartame used in the diet of experimental animals were too large. In doing so, the facts from the study of the DG Sanco Food Scientific Committee on Aspartame Safety for 2002, which claim that ADI of 40 mg/kg body weight is not exceeded by consumers, are taken into account, even more, because at consumers who intake larger amounts of food in which aspartame is added the daily intake does not exceed 10 mg/kg body weight. European Foundation "B. Ramazzini" later, in the statements disagreed with the opinion of EFSA, considering that the quantities of aspartame of 5000 mg, 2500 mg, 1000 mg, 500 mg, 20 mg, 4 mg and 0 mg per kg body weight of rats per day were in fact, those that can be compared with the human daily intake [11].

A second study, conducted in Finland, found that among the majority of additives, including sweeteners, especially in adolescence diabetics, ADI is less than the determined quantities for each sweetener. Nitrites whose daily intake in children reaches between 39-89% ADI are distinguished.

The greatest controversy was caused by papers that linked certain additives (colors and preservatives) to the change in behavior in children. The first papers on this topic were published in 1978, and later in 2004, 2005 and 2007. The McCann research was supported by the UK's Food Standards Agency Scientific Board, which resulted in a request from the European Commission and a quick response from EFSA, opinion of 25 March 2008.

EFSA reported that the above research, which concerned the impact of individual colors (E102, E104, E110, E124, E129, E122) and the E211 preservative on the behavior of children 3 years old and children 8-9 years old, couldn't be taken as a final answer, for several reasons:

1. It does not apply to the whole population, and reliable data on sensitivity to individual colors is not well developed in the study, so it is unclear whether one or more colors (synergistically) caused the registered changes in the behavior of children. The clinical significance of the observed effects is also unclear, because it is not known whether these minor changes can hinder concentration and activities in the performance of school tasks and other intellectual functions.
2. Given the significant uncertainty, such as the lack of consistency and the relatively poor effect and lack of information on the clinical significance of the observed behavioral changes, the EFSA Board, the Panel of Food Additives and Nutrition Sources added to food, concludes that the study can't be the basis for changing ADI or, perhaps, a ban on the respective colors or sodium benzoate.

McCann's study included more than 300 children during the research, which shows that parents were aware that, except for the anticipated observation of hyperactivity, children will not be exposed to other health changes. This, in a way, dismissed the suspicions that certain azo dyes are certainly harmful to health, especially in children. The colors were added in separate drinks, thus the colors were brought into the body during the day.

However, during November 2009, EFSA changed the ADI for the yellow colors Quinolline Yellow (E104) and Sunset Yellow (E110), as well as for the red color Ponceau 4R (E124), but not for the yellow color Tartrazine (E102) and other red colors E122, E129.

The entire study or study of McCann is based on previous research carried out in the second half of the twentieth century, in which there is a strong suspicion that the color Tartrazine (E102) may be associated with hyperactivity in children [12].

3.9 Use of additives from "natural" sources

The question often arises is whether additives for which production are used raw materials from "natural" sources are "safer" than additives for which production are used pure synthesized chemical compounds. In essence, this difference does not exist, since additives found in natural raw materials, as well as additives synthesized by chemical way, are susceptible to a controlled chemical process in their obtaining. Every chemical process, including the cooking of favorite food with natural raw materials, brings with it possible contamination or appearance of harmful substances for the health of people.

Thus, when preparing carbohydrate-rich foods, it is possible to form acrylamide as a result of the interaction of the natural ingredients of food rich in asparagine, essential amino acids and some sugars at high temperatures (> 120ºC). Large quantities in fried potatoes and cereal products were found. The impact of acrylamide, final raw material for some plastics, on health is not clear, and numerous studies are under way to discover possible acrylamide-related diseases.

During the preparation of smoked meat products at lower temperatures, benzopyrene can develop, which can cause stomach cancer, and 3-MCPD, which also has a carcinogenic effect, occurs in heat-treated food, fried cheese or fried cereals, and in soy based sauces.

Natural raw materials contain natural substances, which, depending on the quantities intake and the frequency of consumption, can have a harmful effect on human health. Thus, Garlic *(Allium sativum L.)*, Brown mustard *(Brassica juncea)* and Horseradish *(Cochlearia armoracia)* contain allyl isocyanate, which is associated with tumor formation, bitter almonds *(Prunus amygdalus var. Amara)* contain cyanides, which are known toxins, Basil *(Ocimum basilicum)*, Anise *(Pimpinella anisum)*, Estragon *(Artemisia dracunculus)* contain estragoles that are associated with tumor formation, the sweet root *(Glycyrrhiza glabra)* contains glycyrrhizinic acid which affects the elevated blood pressure and heart rate, the crude mushrooms contain hydrazines that are associated with the appearance of a tumor, the potato contains Solanin, a known toxic substance, spinach contains oxalic acid that causes the formation of stones in the kidney, the shells may contain sacsitoxin, which causes paralysis and death, while some plants contain tannin and tannic acid, which is associated with the onset of cancer of the throat and mouth.

Most of today's additives are a product of the separation of natural ingredients from a food or synthesis of these compounds. The egg contains an excellent emulsifier lecithin (E322), the bark of the apples contains a thickener pectin (E440), acetic acid (E260) is concentrated by vinegar, the ascorbic acid antioxidant (E300) is found in the lemon juice,

a string of thickeners are obtained from algae (E400-E404), trees, plants, natural colors are found in carrots (E160a), grapes (E163), beetroot (E162), green leaves (E140), while sodium bicarbonate (E500) or bakery compound is synthesized from inorganic compounds 210 years ago, as a carbon-dioxide-containing compound and released it when required.

Also, many anti-clotting substances are naturally occurring silicates, such as talc E533, bentonite E558, silicon dioxide E551, calcium silicate E552 and sodium aluminosilicate E554 [13].

When the food has a clear mark "without preservatives", it is desired to point out the "particularity" of the food, although with this the consumer is misled. Any food that contains additives in the prescribed quantities for this food, is healthy and does not differ from other similar foods without added preservatives or some other additives. For example, chemical compounds that are very similar to benzoic acid (E210) can be found in larger quantities in nature in fruits similar to raspberries Scandinavian Cloudberry *(Rubus chamaemorus L.)*, while sorbic acid (E200) can be found in some plants. Sulfur dioxide was used as a preservative in Homer's time (7th and 8th century BC), and today it processes some raw materials for food production, because its antioxidant and conservative effect keeps the product from change and spoilage. Even their presence in traces gives the statement "without preservatives" a suspicion that the manufacturer has not checked his raw materials.

Dimethyl dicarbonate E242 is a preservative that, by the addition to soft drinks or other such drinks, decomposes to methanol and carbon dioxide, previously preventing the enzyme acetate kinase and glutamic acid decarboxylase. This affects the durability of the product. Analytically, it is almost impossible to prove it, and all this can be an incentive for the manufacturer to use the inscription "without preservatives" with certain certainty, although he should not. The words "without preservatives" can also be a negative warning that food is unprotected and can be microbiologically contaminated. Venomes that produce molds and bacteria are the strongest toxins found in food, such as botulinum toxins, Clostridium botulinum (neurotoxic effect) and secondary metabolites of the molds - mycotoxins and, in particular, toxic aflatoxins etc.

The pressure from the public to eject the E-numbered additives from food, often has its own, not very beautiful side, which can be illustrated by the example of colors. Certain food manufacturers wanting to achieve the coloring effect in any way and giving the prefix "natural" to the coloring, consider that with the definition of additives are prevented by replacing synthetic organic colors with "natural" versions. Unlike additives that into the category of colors and have exactly certain parameters of health correctness, as well as quality parameters, "natural" versions do not have this, so they are therefore problematic in assessing the health correctness and quantity that can or may be in the food.

An example is Spirulina, which a company uses as a blue color (candy). Spirulina is usually a name for an extract derived from algae *Arthrospira platensis* and *Arthrospira maxima*. As such, it is associated with foods with a special effect, by attaching positive preventive and active health effects. Apart from that company, the products, the food, are not known, in which spirulina is used to obtain the required color, but the ice cream industry is particularly interested. Pigments and other spirulina substances that give food color are: chlorophyll-a, xanthophyll, beta-carotene, echinenone, myxoxanthophyll, zeaxanthin, canthaxanthin, diatoxanthin, 3'-hydroxyechinenone, beta-cryptoxanthin, oscillaxanthin, phycobiliproteins, c-phycocyanin allophycocyanin [14].

According to the instructions supplied with products containing pure Spirulina in tablets or capsules that are on the market, the daily intake is limited to one tablet per day, and after a certain time the intake increases to 6 tablets per day. Without assuming the final opinion on the use of Spirulina for staining food, several important facts are not known, such as the amount of pure spirulina to be added to the product to receive the required color tone and the possible positive, but also a negative effect on that amount on health.

In addition, natural colors classified in food additives, as well as other sources of natural pigments (such as Spirulina), which, by definition, are not graded in colors, have a basic remark on the stability of the complex foodstuff. Chemical reactivity or the lipophilic nature of natural pigments require additional food processing or to the pigments themselves, such as emulsifying, removing oxygen from the product, protecting against the decline of pigments and protecting against color change in brown. It increases the price of the final product, but it also changes the nature of other important food ingredients.

The sources of natural colors are expensive, and more often with the use of certain microorganisms, colors are synthesized which in composition are almost completely similar to additives, natural colors. This is the case with the anthocyanins (E163), whose common source is the black grape decoction, berries, the red root and some types of vegetables and flowers, but due to the uncertainty of origin, new technological methods for obtaining anthocyanins by fermentation are patented (ChromaDex company). By fermentation, anthocyanins, leucoanthrocytes and anthocyanins can be obtained as mixtures and individually. Their separation is an advantage in creating a color for food, because with a slight change in pH, the shade of the red color changes, which is an advantage over the anthocyanins of natural raw materials. The resulting additives do not have an assessment of the health correctness associated with the technological process of preparation yet.

However, in the new Regulation (EC) no. 1333/2008 [15] it is envisaged that, when the additive is already included in the list of additives, and there is a significant change in the way of production or in use of the inputs or the nanotechnology is applied, the additive is considered a different additive and the need for a new classifying in the list or changing the specifications before placing it on the market.

Anthocyanins, as the most important representatives of natural colors with a red shade, are unstable between pH 3-4, so instead of them or together with them, in order to achieve a stable color over pH 3, natural colors of beta cyanes and betaines are used (E162), obtained from red beets.

Betaines can be stabilized by adding vitamin C (antioxidant) and adding in food with high vitamin C content, but in these cases, anthocyanins found in food become unstable. However, betaines have several weak points, such as an aroma that is

difficult to remove, a possible microbiological contamination that is difficult to remove, since sterilization after the extraction of the beets must not be used to preserve the color. Therefore, alternative sources and replacements for the beets are sought, for that reason are patented ways to extract from the cactus, but, for now, they are not commercially acceptable.
The colors that we can conditionally call natural and found on the list of food additives and give yellow shades are: anato, beta carotene, lutein, a mixture of carotenoids, riboflavin and curcumin, and with a change in concentration, may give yellow to orange color. Research on the production of yellow colors from other sources has spread to some cactuses and by-products in the production of apple drinks, and such a yellow pigment is called POP (phloridizine oxidation product). Purified gives a yellow color at a pH lower than 5 and orange at pH 6. Apart from the mentioned Spirulina, blue color can give certain anthocyanins from different sources in the pH range of 5.5-8.
Various researches have been conducted in France on blue-green pigments of the microalgae responsible for the green color of the oysters they eat. The active substance is called the marenin from the algae *Haslea osteraria*, which, in addition to the specific resistance to color shades under different conditions in the pH range 6-8, has antioxidant properties appropriate to natural antioxidants in food.
The new color definition in Regulation (EC) no. 1333/2008 [16] states that "colors" are substances that give, strengthen or refine the color of food, and cover, in addition to synthetic colors and natural ingredients of food and natural resources, which are not usually taken as food and which are not normally used such as typical food ingredients. Preparations derived from food and other raw materials from natural sources are obtained by physical and/or chemical extraction by selective excretion of the pigment for coloring, which is dominant in relation to food or aromatic constituents.
According to the cited definition of colors, it can be assumed that natural, insufficiently purified products that are not fully in line with the definition of additives, but serve for coloring, will be used for that purpose. According to the above, the color would also be called, for example, the extract from the fruit of the European black elderberry *(Sambucus nigra)*, and in the declaration of such an ingredient would be indicated: a coloring agent: a fruit extract from a elderberry. The extract of berries from the elderberry would faithfully replace other strains of anthocyanins that are naturally associated with blueberries and by adding blueberry aromas (even natural), according to the sensory properties the product would match the expectations of consumers who want blueberries [17].

4. Conclusions

The assessment of the risk for existing additives, changes in the range of additives use, and the expansion of the list of new additives are a consequence of continuous monitoring and new developments in the field of additives. Thus, the basic EU directive has already been replaced by Directive 1333/2008, while changes in other basic regulations are complementary and change over time.
The results of studies that have not directly examined the correlation of intake of food additives in nutrition with harmful effects on human health can not (even in principle) be used to draw conclusions about the relationships between these parameters. The studies that examined these relationships directly noted that there were one or more important methodological limitations.
Strong conclusions about the safety and possible risks of food additives in the general population can not be achieved on the basis of clinical researches. This outcome is in line with the overall estimates of the authoritative institutions, which concluded that the available data are not sufficient to make the necessary determinations.
Despite the inadequacy of the available evidence, many authors of publications are concerned about the amount of food additives in nutrition in populations and subpopulations they have studied, and these concerns have been noted by authoritative bodies.
At the same time, most of these authors offered only qualified conclusions that they expressed occasionally. In addition, the authors of the publications from primary researches, the authors of the reviewed articles and the authoritative institutions call for the implementation of further researches.
It is unclear whether negative findings in laboratory animals can be passed on to health risks in humans, as there are insufficient data on this issue.
Authoritative bodies allow certain food additives that are associated with risks, as long as only small amounts are added. The lack of adequate or no studies in humans and inconsistent results leave many unanswered questions about the dangers of food additives and preservatives.
With varied and moderate foods there are no opportunities for people who feed with industrially processed foods to intake food additives more than the accepted daily quantities. These are amounts that do not affect people's health. This only applies to the healthy population. People who have health problems, depending on the illness or intolerance, themselves or on the advice of their doctor decide whether they will consume or not some food containing a certain additive marked in the food declaration.
In order to give an answer to the question of the impact of additives on health, tests are always carried out using new sensitive analytical methods.

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