



Review Paper

Food Additives as Important Part of Functional Food

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Abstract

The main characteristics and classification of food additives, which are common in the food production, have been described in the present review. The ways of food additives classification, source of nature, mainly antioxidants, food coloring, flavors, flavor enhancers, bulking agents, stabilizers, sweeteners which were collected from literature based on structural and biochemical characteristics with description of source and possible effects on human, organisms and environment have been presented.

Keywords: Food additives, antioxidants, sweeteners, stabilizers, bulking agents, food coloring, flavour enhancers

Introduction

The EC Concerted Action on Functional Food Science in Europe (FUFOSE) proposed a working definition of functional food: a food that beneficially affects one or more target functions in the body beyond adequate nutritional effects in a way that is relevant to either an improved state of health and well-being and/or reduction of risk of disease. It is consumed as part of a normal food pattern. It is not a pill, a capsule or any form of dietary supplement.

Practical examples of a functional food: a natural food such as fruit or grain which may or may not be modified by plant breeding or other technologies (e.g. lycopene-enhanced tomatoes, vitamin E-enriched vegetable oils, vitamin A-enriched rice); a food to which a component has been added (e.g. a spread with added phytosterols); a food from which a component has been removed or reduced (e.g. a yogurt with reduced fat); a food in which one, or several components, have been modified, replaced or enhanced to improve its health properties (e.g. a juice drink with enhanced antioxidant content, a yogurt with added prebiotic or probiotic).

As a Canadian comparison, Health Canada and Agriculture and Agri-Food Canada both define functional foods as, "similar in appearance to – or may be – conventional foods, are consumed as part of a usual diet, and are demonstrated to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions"^{1,2}. Furthermore, functional foods are created through a variety of means, including: fortification with vitamins and/or minerals to provide added

health benefits (e.g. fortified soy beverages and fruit juices with calcium). Addition of bioactive ingredients (e.g., muffins with beta glucan, yogurts with probiotics and drinks with herb blends) or food additives. Bioactive-component enhancement through plant breeding, processing, or special livestock feeding techniques (e.g., omega-3 eggs, milk and meat, canola oil high in carotenoids, and wheat with enhanced lutein levels)¹.

According to Coppens, food supplements were nationally regulated in the EU until 2002, when the Food Supplements Directive 2002/46/EC came into effect². This directive provides a list of the vitamins and minerals that can be used in the manufacture of food supplements³.

In some instances, it is possible to identify and measure markers of health and well-being rather than studying the disease under consideration. Use of properly validated markers demands an understanding of the mechanisms in the attainment of optimal health or disease development. Markers must be scientifically well established and chosen to reflect accurately the processes of interest. Only then can the effect of consuming a functional food on a valid proxy for the final endpoint – i.e. an improved state of health and well-being or reduction in disease risk – be studied³.

Markers could be chosen to reflect: a key target biological function e.g. Bacterial populations in the gut can be measured to demonstrate that a probiotic has successfully passed through the stomach and could potentially have a beneficial effect in the lower GI tract; a key stage in the development of a disease e.g. Bone mineral density can be used as a marker in the study of a

functional food evaluating potential benefit in reducing the risk of osteoporosis; e.g. Flow mediated dilatation (FMD) can be used in the study of a food component designed to improve endothelial function and so reduce the risk of cardiovascular disease. The most known food additives are differ antioxidants, bulking agents, food colouring, flavours, flavor enhancers, glazing agents, stabilizers, sweeteners and the aim of this review is shortly describe main their characteristics and effects on human organism⁴.

Antioxidants

The main anthocyanins in fruits are glycosides of different anthocyanidins, mainly cyanidin, that are widespread and commonly contribute to the pigmentation of fruits. Citrus fruits differ in their flavonoid profiles from other fruit species, containing flavanones and flavones (hesperidin and naringenin) that are not common in other fruits⁴.

The major polyphenolic constituents present in green tea are epicatechin, epigallocatechin, epicatechin-3-gallate and epigallocatechin-3-gallate. In addition to small amount of catechins, black tea contains thearubigins and theaflavins, which are the polymerised forms of catechin monomers and are the major components formed during enzymatic oxidation and the fermentation process⁵. The most abundant catechin in green tea, accounts for 65% of the total catechin content. A cup of green tea may contain 100–200 mg of epigallocatechin-3-gallate. The epicatechin (EC), (–) epicatechin-3-gallate (ECG), (–) epigallocatechin (EGC), (–) epigallocatechin-3-gallate (EGCG), (+) catechin, and (+) galocatechin (GC) are present in higher quantities in green tea than in black or oolong tea, because of differences in the processing of tea leaves after harvest. For green tea, fresh tea leaves from the plant *Camellia sinensis* are steamed and dried to inactivate the polyphenol oxidase enzyme, a process that essentially maintains the polyphenols in their monomeric forms. Black tea, on the other hand, is produced by extended fermentation of tea leaves which results in the polymeric compounds, thearubigins and theaflavins.

Most of the medicinal properties of green tea are associated with the epicatechins rather than the catechins⁶. The green tea catechins have been shown to be more effective antioxidants than vitamins C and E⁷, and their order of effectiveness as radical scavengers is ECG-EGCG-EGC-EC-catechin.

Flavonoids have been reported to possess a wide range of activities in the prevention of common diseases, including CHD, cancer, neurodegenerative diseases, gastrointestinal disorders and others⁸.

Flavonols - are found at high concentrations in onions, apples, red wine, broccoli, tea, and *Ginkgo biloba*⁹. The most common in the American diet are Quercetin (70%), Kaempferol (16%), and Myricetin (6%)^{10,11}.

Quercetin is a flavonoid molecule ubiquitous in nature. Quercetin is a flavonoid that forms the "backbone" for many other flavonoids, including the citrus flavonoids rutin, hesperidin, naringin and tangeritin. In studies, quercetin is found to be the most active of the flavonoids, and many medicinal plants owe much of their activity to their high quercetin content. Quercetin has demonstrated significant anti-inflammatory activity because of direct inhibition of several initial processes of inflammation; respectively it inhibits both the manufacture and release of histamine and other allergic/inflammatory mediators¹². In addition, it exerts potent antioxidant activity¹³ and vitamin C-sparing action. Quercetin and wine polyphenols might be of therapeutic benefit in cardiovascular diseases even though prospective controlled clinical studies are still lacking¹⁴.

A number of its actions make it a potential anti-cancer agent, including cell cycle regulation, interaction with type II estrogen binding sites, and tyrosine kinase inhibition. Quercetin appears to be associated with little toxicity when administered orally or intravenously. Much in vitro and some preliminary animal and human data indicate quercetin inhibits tumor growth. More research is needed to elucidate the absorption of oral doses and the magnitude of the anti-cancer effect.

Isoflavones, respectively genistein, daidzein, glycitein are found in soy and have an influence on bone health among postmenopausal women, together with some weak hormonal effects. Thus, depending on the estradiol concentration, they exhibit weak estrogenic or antiestrogenic activity¹⁵.

Synthetic antioxidants such as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) have been used as antioxidants since the beginning of this century. Restrictions on the use of these compounds, however, are being imposed because of their carcinogenicity¹⁶.

Thus, a need for identifying alternative natural and safe sources of food antioxidant is created¹⁷ and the search for natural antioxidants, especially of plant origin, has notably increased in recent years¹⁸.

In particular, the hydroxybenzoic acid protocatechuic acid (PCA) has been eliciting a growing interest for several reasons. Firstly, PCA is one of the main metabolites of complex polyphenols such as anthocyanins and procyanidins that are normally found at high concentrations in vegetables and fruit, and are absorbed by animals and humans. Since the daily intake of anthocyanins has been estimated to be much higher than that of other polyphenols, the nutritional value of PCA is increasingly recognized. Secondly, a growing body of evidence supports the concept that PCA can exert a variety of biological effects by acting on different molecular targets. It has been shown that PCA possesses antioxidant, anti-inflammatory as well as antihyperglycemic and neuroprotective activities. Furthermore, PCA seems to have chemopreventive potential because it inhibits the in vitro chemical carcinogenesis and

exerts pro-apoptotic and anti-proliferative effects in different tissues¹⁹.

Sweeteners

Nowadays the most known from sweeteners additives are glycosides stevioside from plants *S. rebaudiana*. Leaf extract of *S. rebaudiana* promotes effects on certain physiological systems such as the cardiovascular and renal and influences hypertension and hyperglycemia. The chemistry of *Stevia* leaf extracts that are safe to use and having antimicrobial, antibacterial, antiviral and anti-yeast activity²⁰. These activities may be correlated with the presence of antioxidant compounds²¹. More recently, purified extracts of *S. rebaudiana* (Bertoni) Bertoni (Compositae) containing the sweet *ent*-kaurane-type diterpene glycosides stevioside and rebaudioside A have become popular as "dietary supplements"²². Sweetness of 1.0 g of dry stevia leaves in 100 ml water was equivalent to a sucrose solution containing 20 g of sucrose. The antioxidant activity of the extracts of *Stevia* was synergistic when it was mixed with coffee and lime juice. Complete purification of *Stevia* leaf extracts to obtain pure glycosides is not necessary for it to become a commercially acceptable sweetener.

Stabilizers

Stabilizers, thickeners and gelling agents, like agar or pectin (used in jam for example) give foods a firmer texture. While they are not true emulsifiers, they help to stabilize emulsions. Pectic substances are complex high molecular mass glycosidic macromolecules found in higher plants. They are present in the primary cell wall and are the major components of the middle lamellae, a thin extracellular adhesive layer formed between the walls of adjacent young cells. In short, they are largely responsible for the structural integrity and cohesion of plant tissues²³. Pectinases are a big group of enzymes that break down pectic polysaccharides of plant tissues into simpler molecules like galacturonic acids and their production occupies about 10% of the overall manufacturing of enzyme preparations. Pectinolytic enzymes are widely used in the food industry for juice and wine production²⁴. Since pectic substances are a very complex macromolecule group, various pectinolytic enzymes are required to degrade it completely. These enzymes present differences in their cleavage mode and specificity being basically classified into two main groups that act on pectin "smooth" regions or on pectin "hairy" regions²⁵.

In the same time a valuable byproduct that can be obtained from fruit wastes is pectin. Pectin designates those water soluble pectinic acid (colloidal polygalacturonic acids) of varying methyl ester content and degree of neutralization, which are capable of forming gels with sugar, and acids, under suitable condition²⁶. It is used in pharmaceutical preparation as filler, as an agglutinator in blood therapy and also to glaze candied fruits. Besides, it can be used to increase the foaming power of gases in water.

The dominant and unifying structural feature in pectins is a linear 1,4- α linked D-galactopyranosyl uronic acid chain. Pectin, which is a partly esterified polygalacturonide, contains 10 percent or more of organic materials, composed of arabinose, galactose or sugars. AUA (%) is essential to determine the purity and degree of esterification and to evaluate physical properties²⁷. The higher galacturonic acid and lower ash content are the two criteria governing its purity²⁸.

It is evident from the data generated on AUA % of pectin from different fruit wastes (Table 2) that purest pectin could be obtained from mangosteen rind and lime peel, compared to other sources. The AUA% for mangosteen rind pectin was 73.16 and for lime peel pectin, it was 72.5%. Among these two, mangosteen is a weaker source of pectin, whereas lime peel is the commercial source. The value of AUA % obtained for lime peel pectin is approximately same as that reported by Sudhakar and Maini, which was 71.2 per cent²⁹.

All the sugars viz, arabinose, galactose, galacturonic acid and rhamnose, which are structural components of pectin, have free hydroxyl groups (-OH) that can be methylated to form methoxyl groups (-OCH₃) (methylation). Depending upon the degree of methylation, the methoxyl content of pectin varies. The spreading quality and gel grade of pectin are dependent of their methoxyl content. Gel grade is the weight of sugar with which one part by weight of pectin will, under suitable conditions, form a satisfactory jelly. This is the most important character that determines the value of pectin in international market. As the methoxyl content increases the spreading quality and sugar binding capacity of pectin increase.

Pectins from passion fruit rind with methoxy content 4.96% recorded low gel grade (73). Gel grade was in the range of 100 to 200 for those having methoxy content in between seven and eight per cent³⁰.

Properties of pectin in cell walls are sometimes modified by low levels of hydroxyl esterification with acetyl groups. The distribution of acetyl groups in pectin is unknown but in sugar beet, pear and apricot pectin, acetyl levels are reported to approach four per cent.

Bulking Agents

Bulking agents such as starch are additives that increase the bulk of a food without affecting its nutritional value. Starch or amylopectin is a carbohydrate consisting of a large number of glucose units joined by glycosidic bonds. This polysaccharide is produced by all green plants as an energy store. It is the most common carbohydrate in the human diet and is contained in large amounts in such staple foods as potatoes, wheat (75%), maize (corn) (72%), rice (86%), and the root vegetables (potatoes (24%) and cassava) (table 1)³¹.

Table-1
Content of starch in different plants

Name of plant	Part of plant	Content of starch	Content of sugar
Typha latifolia	dried rhizome	58 % (25-58%)	10%
Cetraria islandica	Vegetation part	Near 44% of lichen	-
Glyceria	Weevil	75%	-
Zea mays L.	Seeds	71%	-
Artocarpus altilis	dried pulp	80 % (60-80%)	14%
Nymphaea alba	Rhizome	40%	20,00%
Avena	Grain	60%	-
Butómus umbellátus	Rhizome	60%	-
Trapa natans and Trapa bispinosa	Nut	55%	-
Ipomoea batatas L.	Tubers	72%	-
Sorghum	-	74%	-
Manihot	-	77%	-
Pisum	grain	40%	-
Hordeum L.	grain	75%	-
Solanum tuberosum	tubers	82%	-
Oryza	grain	89%	-
Secale	grain	72%	-
Triticum L.	grain	74%	-
Althaea officinalis L.	roots	37%	10%
Sagittaria sagittifolia L.	tubers	35%	-

Pure starch is a white, tasteless and odorless powder that is insoluble in cold water or alcohol. It consists of two types of molecules: the linear and helical amylose and the branched amylopectin. Depending on the plant, starch generally contains 20 to 25% amylose and 75 to 80% amylopectin by weight³². Glycogen, the glucose store of animals, is a more branched version of amylopectin.

Starch is processed to produce many of the sugars in processed foods. Dissolving starch in warm water gives wheatpaste, which can be used as a thickening, stiffening or gluing agent. The biggest industrial non-food use of starch is as adhesive in the papermaking process.

A modified starch is a starch that has been chemically modified to allow the starch to function properly under conditions frequently encountered during processing or storage, such as high heat, high shear, low pH, freeze/thaw and cooling. The modified food starches are E coded according to the International Numbering System for Food Additives (INS)³³: 1400 Dextrin, 1401 Acid-treated starch, 1402 Alkaline-treated starch, 1403 Bleached starch, 1404 Oxidized starch, 1405 Starches, enzyme-treated, 1410 Monostarch phosphate, 1412 Distarch phosphate, 1413 Phosphated distarch phosphate, 1414

Acetylated distarch phosphate, 1420 Starch acetate, 1422 Acetylated distarch adipate, 1440 Hydroxypropyl starch, 1442 Hydroxypropyl distarch phosphate, 1443 Hydroxypropyl distarch glycerol, 1450 Starch sodium octenyl succinate, 1451 Acetylated oxidized starch.

Food Coloring

Food coloring, or color additive, is any dye, pigment or substance that imparts color when it is added to food or drink. They come in many forms consisting of liquids, powders, gels and pastes. Food coloring is used both in commercial food production and in domestic cooking. Color additives are used in foods for many reasons including offset color loss due to exposure to light, air, temperature extremes, moisture and storage conditions, correct natural variations in color enhance colors that occur naturally, provide color to colorless and "fun" foods.

Color additives are recognized as an important part of many foods we eat. Some of the food colorings have the abbreviation "FCF" in their names. This stands for "For Coloring Food" (US)³⁴ or "For Coloring of Food" (UK)³⁵ (table 2.)

Table-2
Classification of coloring³⁶

Natural food dyes	Artificial coloring			
Caramel coloring (E150), made from caramelized sugar	FCF	Limited use	Delisted and banned	Food coloring in the EU
Annatto (E160b), a reddish-orange dye made from the seed of the achiote.	FD&C Blue No. Brilliant Blue FCF, E133 (blue shade)	Orange B (red shade) - allowed only for use in hot dog and sausage casings.	FD&C Red No. 2 – Amaranth	Quinoline Yellow: E104
Chlorophyllin (E140), a green dye made from chlorella algae	FD&C Blue No. 2 – Indigotine, E132 (indigo shade)	Citrus Red 2 (orange shade) - allowed only for use to color orange peels.	FD&C Red No. 4	Carmoisine: E122
Cochineal (E120), a red dye derived from the cochineal insect, <i>Dactylopius coccus</i>	FD&C Green No. 3 –Fast Green FCF, E143 (turquoise shade)	-	FD&C Red No. 32 was used to color Florida oranges	Ponceau 4R: E124
Betanin (E162) extracted from beets	FD&C Red No. 40–Allura Red AC, E129 (red shade)	-	FD&C Orange Number 1 was one of the first water soluble dyes to be commercialized, and one of seven original food dyes allowed under the Pure Food and Drug Act of June 30, 1906	Patent Blue V: E131
Turmeric (curcuminoids, E100)	FD&C Red No. 3 – Erythrosine, E127 (pink shade, commonly used in glacé cherries)	-	FD&C Orange No. 2 was used to color Florida oranges	Green S: E142
Saffron (carotenoids, E160a)	FD&C Yellow No. 5–Tartrazine, E102 (yellow shade)	-	FD&C Yellow No. 1, 2, 3, and 4	-
Paprika (E160c) Lycopene (E160d) Elderberry juice Pandanus (<i>Pandanus amaryllifolius</i>), a green food coloring Butterfly pea (<i>Clitoria ternatea</i>), a blue food dye	FD&C Yellow No. 6–Sunset Yellow FCF, E110 (orange shade)	-	FD&C Violet No. 1	-

Flavor Enhancers

Flavor enhancers are food additives commonly added to food and designed to enhance the existing flavors of products³⁷. When flavor compounds are added to foods, no health hazards should arise from the concentrations used. The flavor contains

flavoring substance and solvents or carries; the concentration of a single flavoring substance in the food does not usually exceed 10-20 ppm. The commonly used flavour enhancers are by Australian and European (by E number) classification (table 3.).

Table-3
Flavour enhancers are by Australian and European (by E number) classification

Australian	European (by E number)
620 glutamic acid	Glutamic acid (an amino acid) and its salts: E620 Glutamic acid E621 Monosodium glutamate, MSG E622 Monopotassium glutamate E623 Calcium diglutamate E624 Monoammonium glutamate E625 Magnesium diglutamate
621 monosodium glutamate, MSG	Guanylic acid (a ribonucleotide) and its salts: E626 Guanylic acid E627 Disodium guanylate, sodium guanylate E628 Dipotassium guanylate E629 Calcium guanylate
622 monopotassium glutamate	Inosinic acid (a ribonucleotide) and its salts: E630 Inosinic acid E631 Disodium inosinate E632 Dipotassium inosinate E633 Calcium inosinate
623 calcium diglutamate	Mixtures of guanylate and inosinate: E634 Calcium 5'-ribonucleotides E635 Disodium 5'-ribonucleotides
624 monoammonium glutamate	Maltol and ethyl maltol: E636 Maltol E637 Ethyl maltol
625 magnesium diglutamate 627 disodium 5'-guanylate 631 disodium 5'-inosinate 635 disodium 5'-ribonucleotides 636 maltol 637 ethyl maltol 640 glycine 641 l-leucine	Amino acids and their salts: E640 Glycine and its sodium salt E641 L-Leucine

Flavoring substances is the general name given to certain substances that possess no nutritional properties and are used to improve the taste and aroma of food. Flavoring substances include spices, such as mustard, pepper, clove, bay leaf, caraway, dill, cardamom, ginger, vanilla, and cinnamon; food acids, such as acetic, citric, tartaric, and malic; and aromatic essences. When ingested with food, flavoring substances (especially spices) stimulate the olfactory and gustatory nerves, which in turn intensify salivation and secretion of gastric and pancreatic juices. Flavoring substances directly stimulate the mucous membrane of the digestive tract thereby increasing the flow of digestive juices, which improve the appetite as well as the digestion and assimilation of food³⁸.

For flavoring preparations sold by retail, the carriers, diluents, solvents and other additives present in the flavoring product are required to be declared as ingredients on the label if they are

performing a technological function in that food (i.e. they are acting as food additives not present as processing aids). The classification which is regarding nature of flavoring substances is presenting 4 differ classes of substances: natural, nature-identical, artificial and smoke flavoring substances³⁹.

Natural flavoring substances means flavoring substances obtained from plant or animal raw materials, by physical, microbiological or enzymatic processes. They can be either used in their natural state or processed for human consumption, but cannot contain any nature-identical or artificial flavoring substances.

Nature-identical substances means flavoring substances that are obtained by synthesis or isolated through chemical processes, which are chemically identical to flavoring substances naturally present in products intended for human consumption. They cannot contain any artificial flavoring substances.

Artificial flavoring substances means flavoring substances not identified in a natural product intended for human consumption, whether or not the product is processed. Artificial flavoring substances which are aromatic substances not found in the natural product for human consumption (whether or not processed)⁴⁰. There are fewer varieties of such flavoring substances because they are made by chemical synthesis with the chemical structure which does not exist in the natural world. Based on this, the safety of these flavoring substances is a cause for great concern. In China, the flavoring substances listed in the GB / T 14156-1993 "Foods Flavors and Coding" are considered harmless to human body (with certain dosage) after the evaluation of toxicology. Except individual varieties through the sufficient toxicology evaluation, they are currently allowed to be used temporarily.

As example a strawberry-flavored milk could contain as natural flavoring substances, whether derived from strawberries and not; a nature-identical flavoring substance that has been synthesized, but is chemically identical to a substance found in nature (like cyclodextrins), or an artificial flavor, that has been

synthesized and has not yet been identified in any natural product⁴¹.

For example cyclodextrins (CDs) are cyclic oligomers widely used in the food industry as food additives, for stabilization of flavors, for elimination of undesired tastes or other undesired compounds such as cholesterol and to avoid microbiological contaminations and browning reactions⁴². Cyclodextrins are produced from starch by means of enzymatic conversion. α -CD is food additive E459 and widely used in food technology production.

Smoke flavoring is a natural flavoring concentrate obtained by subjecting untreated and uncontaminated hardwood, including sawdust and woody plants, to one or more of the following processes (controlled burning, dry distillation at appropriate temperatures and/or treatment with superheated steam) and obtaining fractions which have the desired flavor potential. Flavor enhancers are food additives commonly added to food can have differ effect (table 4).

Table-4
Nature of flavor enhancers and their effects

Number	Name	Characteristics
620 E620	Glutamic acid	Natural amino acid (building block of protein). Commercially prepared from molasses by bacterial fermentation. Also prepared from vegetable protein, such as gluten, or soy protein. Glutamic acid and glutamates are present in all proteins. Free glutamates are present in high concentrations in ripened cheese, breast milk, tomatoes and sardines. Flavor enhancer, salt substitute used in sausages, seasoning, savory snacks - many savory foods. An amino acid present in many animal and vegetable proteins, derived commercially from bacteria; might cause similar problems as MSG (621), young children should avoid it. It could kill nerve cells, resulting in diseases such as Huntington's, Alzheimer's and Parkinson's ⁴³
621 E621	Monosodium L-glutamate (MSG)	Sodium salt from glutamic acid (E620), a natural amino acid (building block of protein). Commercially prepared from molasses by bacterial fermentation. Added to any savory processed protein food. In cigarettes and animal food. In over 10,000 foods in USA. Flavour enhancer derived from the fermentation of molasses, salt substitute; adverse effects appear in some asthmatic people, should not be permitted in foods for infants and young children as it could damage the nervous system. Typical products are canned vegetables, canned tuna, dressings, many frozen foods. To be avoided. It could kill nerve cells, resulting in diseases such as Huntington's, Alzheimer's and Parkinson's. Pregnant women, children, hypo-glycemic, elderly and those with heart disease are at risk from reactions. 71 healthy subjects were treated with placebos and monosodium L-glutamate (MSG) doses of 1.5, 3.0 and 3.15 g/person, which represented a body mass-adjusted dose range of 0.015-0.07 g/kg body weight before a standardized breakfast over 5 days. A significant (P < 0.05) negative correlation between MSG dose and after-effects was found. The profound effect of food in negating the effects of large MSG doses was demonstrated ⁴⁴ .
622 E622	Monopotassium L-glutamate	Potassium salt from glutamic acid (E620), a natural amino acid (building block of protein). Commercially prepared from molasses by bacterial fermentation. Also prepared from vegetable protein, such as gluten, or soy protein. Less used and not as salty, low sodium salt substitute. Can cause nausea, vomiting, diarrhoea, abdominal cramps; typical products are low sodium salt substitutes. Not for babies less than 12 months old or those people with impaired kidneys ⁴⁵ .
623	Calcium di-L-	Commercially prepared from molasses by bacterial fermentation. Also prepared from vegetable

E623	glutamate	protein, such as gluten, or soy protein. Salt substitute, no known adverse effects, but possible problems for asthmatics and aspirin sensitive people.
624 E624	Monoammonium L-glutamate	Commercially prepared from molasses by bacterial fermentation. Also prepared from vegetable protein, such as gluten, or soy protein. Salt substitute, flavor enhancer. No known adverse effects.
625 E625	Magnesium di-L-glutamate	Commercially prepared from molasses by bacterial fermentation. Also prepared from vegetable protein, such as gluten, or soy protein. Salt substitute, flavor enhancer. Hardly used, only in low sodium meat products. No known adverse effects.
E626	Guanylic acid	Not listed for use in Australia. Guanylic acid is a natural acid, which is part of RNA, one of the genetic carrier molecules in the cell. It is thus part of all cells in all living organisms. Commercially prepared from yeast extract or sardines. Asthmatic people should avoid guanylic acid and guanylates. As guanylates are metabolized to purines, they should be avoided by people suffering from gout. Guanine nucleotides may be utilized to a greater degree during severe stress and administration of exogenous guanine nucleotides may produce more effective protein anabolism under these circumstances ⁴⁶ .
627 E627	Disodium guanylate	Flavor enhancer. Isolated from sardines or yeast extract; not permitted in foods for infants and young children. Persons with gout, hyperactivity, asthmatics and aspirin sensitive's should avoid it. It is found in instant noodles, potato chips and snacks, savory rice, tinned vegetables, cured meats, packet soup. Glucose is oxidized quantitatively to carbon dioxide with hydrogen peroxide ⁴⁷ in the presence of disodium phosphate which can may oxidative effect later; in the absence of the latter no oxidation occurs or only very slowly. Warburg and Yabusoe ⁴⁸ found that fructose in the presence of disodium phosphate is oxidized by atmospheric oxygen, while glucose is not thus affected.
E628	Dipotassium guanylate, 5'-	Flavor enhancer. Guanylic acid and guanylates do not have the specific umami taste but strongly enhance many other flavours, thereby reducing the amounts of salt needed in a product. Asthmatic people should avoid guanylic acid and guanylates. As guanylates are metabolised to purines, they should be avoided by people suffering from gout. However, the concentrations used are generally so low that no effects are to be expected. Guanylic acid and guanylates are generally produced from yeasts, but partly also from fish. They may thus not suitable for vegans and vegetarians.
E629	Calcium guanylate	Calcium salt of guanylic acid (E626), a natural acid, which is part of RNA, one of the genetic carrier molecules in the cell. It is thus part of all cells in all living organisms. Commercially prepared from yeast extract or sardines. Flavour enhancer. Guanylic acid and guanylates do not have the specific umami taste but strongly enhance many other flavours, thereby reducing the amounts of salt needed in a product. Used in many products, mainly in low-salt/sodium products. Acceptable daily intake (ADI): None determined. Guanylates may not be used in products intended for children under 12 weeks. Asthmatic people should avoid guanylic acid and guanylates. As guanylates are metabolised to purines, they should be avoided by people suffering from gout.
E630	Inosinic acid	A natural acid, that is mainly present in animals. Commercially prepared from meat or fish (sardines). May also be produced by bacterial fermentation of sugars. Used by athletes to supposedly increase the oxygen capacity of their blood. Used in many products. The extraneous inosinic acid addition may contribute to the improvement of growth, meat quality, and deposition of inosinic acid in broilers ⁴⁸ . Acceptable daily intake (ADI): None determined. Inosinates may not be used in products intended for children under 12 weeks. Asthmatic people should avoid inosinates. As inosinates are metabolised to purines, they should be avoided by people suffering from gout. Inosinates are generally produced from meat, but partly also from fish. They are thus not suitable for vegans and vegetarians, and in most cases not suitable for Jews, Muslims and Hindus, depending on the origin of the product. Only the producer can provide information on the origin.
631	Disodium inosinate	May be prepared from meat or sardines; not permitted in foods for infants and young children.

E631		Gout sufferers avoid. It is found in instant noodles, potato chips and snacks, savoury rice, tinned vegetables, cured meats, packet soup. Asthmatic people should avoid inosinates. As inosinates are metabolised to purines, they should be avoided by people suffering from gout. Frequently contains MSG (621)
E632	Dipotassium inosinate	Potassium salt of inosinic acid (E630), a natural acid, that is mainly present in animals. Commercially prepared from meat or fish (sardines). May also be produced by bacterial fermentation of sugars. Flavour enhancer. Inosinic acid and inosinates do not have the specific umami taste but strongly enhance many other flavours, thereby reducing the amounts of salt or other flavour enhancers needed in a product ⁴⁹ . Used in many products. Mainly used in low sodium/salt products. Acceptable daily intake (ADI): None determined. Inosinates may not be used in products intended for children under 12 weeks. Asthmatic people should avoid inosinates. As inosinates are metabolised to purines, they should be avoided by people suffering from gout. However, the concentrations used are generally so low that no effects are to be expected. Inosinates are generally produced from meat, but partly also from fish. They are thus not suitable for vegans and vegetarians, and in most cases not suitable for Jews, Muslims and Hindus, depending on the origin of the product. Only the producer can provide information on the origin.
E633	Calcium inosinate	Calcium salt of inosinic acid (E630), a natural acid, that is mainly present in animals. Commercially prepared from meat or fish (sardines). May also be produced by bacterial fermentation of sugars. Flavour enhancer. Inosinic acid and inosinates do not have the specific umami taste but strongly enhance many other flavours, thereby reducing the amounts of salt or other flavour enhancers needed in a product. Used in many products. Mainly used in low sodium/salt products. Acceptable daily intake (ADI): None determined. Inosinates may not be used in products intended for children under 12 weeks. Asthmatic people should avoid inosinates. As inosinates are metabolised to purines, they should be avoided by people suffering from gout. However, the concentrations used are generally so low that no effects are to be expected. Soluble guanylate cyclase activity of brain is stimulated by Ca ²⁺ in the presence of low concentrations of Mn ²⁺ . Unlike Ca ²⁺ stimulation of adenylate cyclase, the effect does not depend upon interaction of guanylate cyclase with a specific high-affinity Ca ²⁺ -binding protein ⁵⁰ .
E634	Calcium 5'-ribonucleotides	Mixture of calcium salts of guanylic (E626) and inosinic acid (E630). Flavour enhancer. Guanylates and inosinates do not have the specific umami taste but strongly enhance many other flavours, thereby reducing the amounts of salt or other flavour enhancers needed in a product. Used in many products. Mainly used in low sodium/salt products. Acceptable daily intake (ADI): None determined. Guanylates and inosinates may not be used in products intended for children under 12 weeks. Asthmatic people should avoid guanylates and inosinates. As guanylates and inosinates are metabolised to purines, they should be avoided by people suffering from gout. However, the concentrations used are generally so low that no effects are to be expected ⁵¹ .
635 E635	Disodium 5'-ribonucleotide	Made from 627 and 631. Check imported foods. May be associated with itchy skin rashes up to 30 hours after ingestion; rashes may vary from mild to dramatic; the reaction is dose-related and cumulative, some individuals are more sensitive than others; typical foods include flavoured chips, instant noodles and party pies. Avoid it, especially gout sufferers, asthmatics ⁵¹ and aspirin sensitive people.
E635	Sodium 5'-ribonucleotide	Mixture of sodium salts of guanylic (E626) and inosinic acid (E630). Check imported foods. May be associated with itchy skin rashes up to 30 hours after ingestion; rashes may vary from mild to dramatic; the reaction is dose-related and cumulative, some individuals are more sensitive than others; typical foods include flavoured chips, instant noodles and party pies. Avoid it, especially gout sufferers, asthmatics and aspirin sensitive people. Banned in Australia. Treatment disodium 5'-ribonucleotide on reproductive function over three generations in the rat did not appear to affect parent animals and significant changes in next generation (as assessed by the incidence of mortality, bodyweight change, food consumption, mating performance, pregnancy rate, gestation period, and post-mortem findings) ⁵² .

636 E636	Maltol	Derived from the bark of larch trees, pine needles, chicory wood, oils and roasted malt; it may be produced synthetically. Artificial sweetener, flavour enhancer used in baked goods to give a 'fresh baked' taste and smell in bread and cakes, chocolate substitute, soft and fizzy drinks, ice cream, jam. In large quantities it can help aluminum pass into the brain to cause Alzheimer's disease. Sometimes lactose (from cow's milk) is used. It should thus be avoided by vegans. It does not contain lactose and can be used by lactose-intolerant people. Acceptable daily intake (ADI): Up to 2 mg/kg bodyweight. Some countries ban it for babies and young children. The results of experiment with neuro-protective effect of maltol on oxidative damage in the brain of mice challenged with kainic acid are suggested to be a functional agent to prevent the oxidative damage in the brain of mice ⁵³
637	Ethyl maltol	Derived from maltol chemically. It is related to the more common flavorant maltol by replacement of the methyl group by an ethyl group ³⁰ . Needs more testing. Base for essences, synthetic artificial flavour and flavour enhancer. Sometimes lactose (from cow's milk) is used. It should thus be avoided by vegans. It does not contain lactose and can be used by lactose-intolerant people. Some countries ban it for babies and young children. Acceptable daily intake (ADI): Up to 2 mg/kg bodyweight. In same time the pyrones, maltol and ethyl maltol, are able to enhance the initial stages of iron uptake from the intestinal lumen, possibly by holding the iron in a readily absorbable form, but do not influence subsequent iron distribution and so may provide safe and palatable alternatives to those iron preparations presently available for the treatment of iron deficiencies ⁵⁴ .
640 E640	Glycine (and its sodium salts), glycol, amino acetic acid	Flavour modifier. Glycine is a natural amino acid, a building block of protein ⁵⁵ . Mainly produced from gelatin, partly synthetic. It is a nutrient, mainly for yeast in bread. Also used as a bread enhancer. Genetically coded amino acid used in dietary supplements. Can be mildly toxic if ingested Glycine is responsible, at least in part, for the ability of this amino acid to ameliorate cisplatin nephrotoxicity ⁵⁶ . Glycine is produced mainly from gelatin, which is derived from animal bones. It is therefore not suitable for vegans, vegetarians. Only the producer can provide the origin of the product.

Conclusion

The review demonstrates that nowadays is presented many differ plants sources of food additives with natural origin and also artificial food additives. However, the review points out a series of aspects which warrant attention e.g. that many substances have not been re-assessed for many years, although new data are accumulating in the scientific literature and in certain cases calls for a new assessment of their effects on human health. It is recommended that a mechanism be put in place in EU, which ensures a systematic, periodic review of all permitted food additives. In the meantime it is suggested to use the data in the present review as help for to know common situation with food additives as some part of functional food system.

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