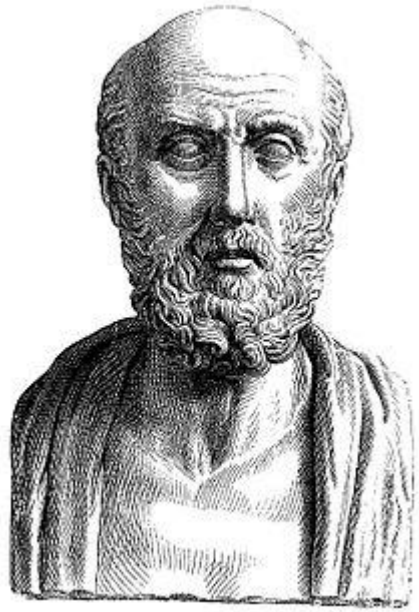
Medical Botany

13. Nutraceuticals



HIPPOCRATES

"LET FOOD BE THY MEDICINES"

Definition- part 1

- Defined as “a foodstuff (as a fortified food or dietary supplement) that provides health benefits in addition to its basic nutritional value.”

- Dr. Stephen DeFelice coined (1989) the term “nutraceutical” from the words nutrition and pharmaceutical and defined it as “a food (or part of a food) that provides medical or health benefits, including the prevention and/or treatment of a disease.”

Full definition

- A substance that is cultivated/produced/extracted or synthesized under optimal and reproducible conditions and, when administered orally to patients, would provide the nutrient(s) required for bringing altered body structure and function back to normal, thus improving the health and well-being of the patients

According to the North American Veterinary Nutraceutical Council

- veterinary nutraceutical is defined as “a substance which is produced in a purified or extracted form and administered orally to patients to provide agents required for normal body structure and function and administered with the intent of improving the health and well-being of animals

Functional food v/s Nutraceutical

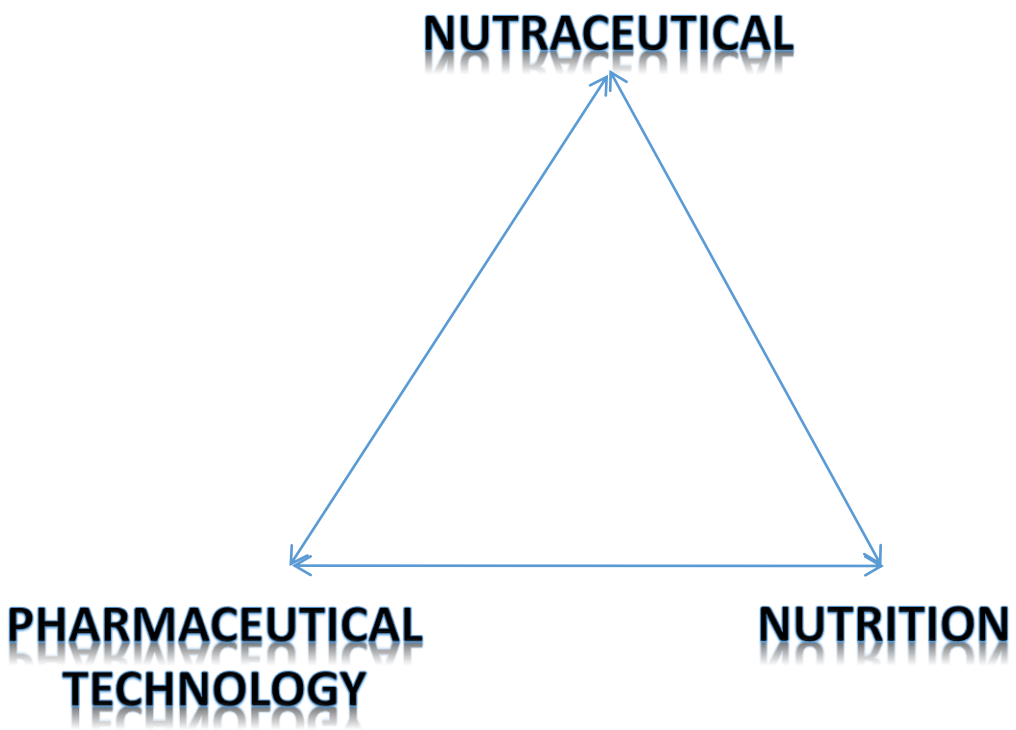
Functional food	Nutraceutical
• Prepared by the aid of 'scientific intelligence' using definite knowledge about its anticipated merit/ usefulness.	• Essentially provides distinct health & medicinal benefits, even including prevention & treatment of perticular disease.
• Vegetables, rice, wheat, fruits, fish, eggs, beaf, meat etc.	• Milk powder, baby food, orange juice, grape juice etc.

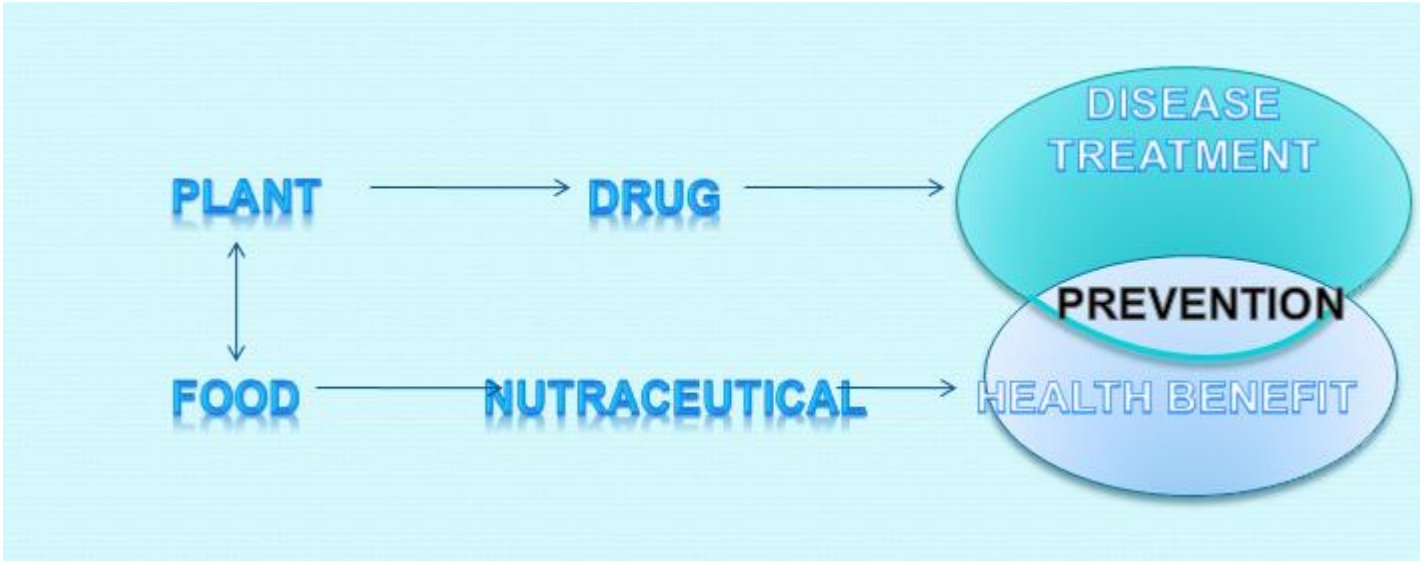
★ FUNCTIONAL FOOD

The food, which is used for the benefit of the human being without knowing the exact effect of food , what and how? is called functional food.

★ NUTRACEUTICALS-

When functional food is used for the treatment or prevention of disease(s) other than anemia it is called Nutraceuticals.


NUTRACEUTICAL
PHARMACEUTICAL TECHNOLOGY
NUTRITION


PLANT
DRUG
DISEASE TREATMENT
PREVENTION
FOOD
NUTRACEUTICAL
HEALTH BENEFIT

Established nutraceuticals-

.Probiotic
.Prebiotic
.Dietary fibre
.Omega 3 fatty acids.
.anti oxidants.

Classification: based on their source

Source	Nutraceuticals
Plant	Tomato, Garlic , Momordica
Animal	Shark liver oil, Code liver oil
Mineral	Calcium, Magnesium, phosphorous
Microorganism	Bifidobacterium, Lactobacilli

Classification: based on their use in disease

Condition	Nutraceuticals
Allergy relief	Ginkgo biloba
Arthritis support	Glucosamine
Cancer prevention	Flax seed, green tea
Cholesterol lowering	Garlic
Digestive support	Digestive enzyme
Diabetic support	Garlic, momordica
Female hormone support	Black cohosh, flash unicorn
Immunomodulator	Ginseng
Prostate support	Tomato lycopenes

Classification: based on their chemicals groupings

Class	Example
Inorganic mineral supplements	Minerals
Vitamin supplement	Vitamins
Digestive enzymes	Enzymes
Probiotics	Helpful bacteria
Prebiotics	Digestive enzymes
Dietary fibres	Fibres
Creals & grains	Wheat, soyabean

Class	Example
Health drinks	Fruit juice and vitamins
Antioxidants	Natural antioxidants
Phytochemicals	
a) Fatty acids	Omega-3-fatty acid
b) Isoprenoids	Carotenoids
c) Lipids	Spingolipids

EXAMPLES OF FUNCTIONAL COMPONENTS

Class / components	Source	Potential benefit
1. Fatty acids CLA	Milk & Meat	Improve body composition, reduce cancers
n-3 FA(DHA, EPA)	Fish oils, berseem & maize fodder,mustard,linseed,rapeseed	Reduce CVD & improve mental, visual function

EXAMPLES OF FUNCTIONAL COMPONENTS

Class / components	Source	Potential benefit
2. Polyphenols		
Anthocyanidine	Fruits	Nutralises free radicals, reduce risk of cancer
Catechins	Tea,babul pods,mustard cake,rape seed,salseed	
Flavonone	Citrus	
Flavones	Fruits, vegetables,soya bean	
proanthocyanidine	Cocoa, chocolate,tea,rape seed	Reduce CVD

3. Saponins	Soybeans,GNC,lucerne,chick pea	Lower cholesterol, anti cancer
4.Probiotics / Prebiotics / Synbiotics		
Lactobacillus	Dahi,yogurt	Improve GI health
Fructo - oligosaccharides	Whole grains, onions, combination of Pro & Prebiotics	

5.Phytoestrogen		
Daidzein , Zenistein	Soybean, flax, lentilseed,maize, berseem,lucerne,subabul fodder	Reduce menopause symptoms, ↑ bone health
Lignans	Flax,rye, vegetables	Reduce cancer and heart diseases

6.Caroteinoids		
β- caroteine	Berseem,lucerne ,oat & maize fodder, Carrots, vegetabels,fruits	Nutralises free radicals
Luteine	vegetabels	Healthy vision
Zeoxanthine	Eggs,citrus,corn	
Lycopene	Tomatoes	Reduce prostate cancer
7.dietary fiber		
Insoluble fiber	Wheat bran	Reduce breast, colon cancer
β-glucan	Oats	Reduce CVD
Whole grain	Cereal grains	

Examples of Functional Food Components of NUTRCEUTICAL

Carotenoids

Functional components	Source	Potential benefits
Alpha-carotene/Beta-carotene	**Carrots, Fruits, Vegetables**	**Neutralize free radicals, which may cause damage to cells**
Lutein	**Green vegetables**	**Reduce the risk of mascular degeneration**
Lycopene	**Tomato products (ketchup, sauces)**	**Reduce the risk of prostate cancer**

Source: International Food Information Council

Lycopene is a phytochemical (phyto - plant) that gives tomatoes their red color and appears to offer potential health benefits. Lycopene is the most potent free radical scavenger of all the caretonoids. It is four times powerful than Alpha-carotene regarding its anti carcinogenic effect on endometrial cells.

- **Supports cardiovascular health**
- **Supports prostate health**
- **Helps prevent DNA and cell damage**
- **Supports healthy and radiant skin**

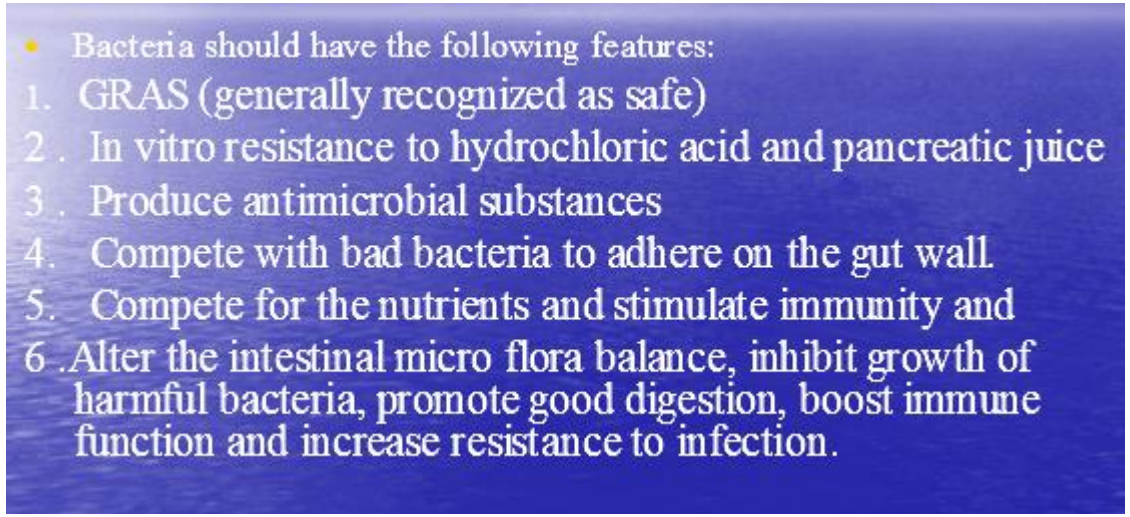
Prebiotics/Probiotics

1. Fructo-oligosaccharides (FOS)	1. Jerusalem artichokes, shallots, onion powder	Improve quality of intestinal microflora; gastrointestinal health
1. Lactobacillus	1. Yogurt, Other dairy	Improve quality of intestinal microflora; gastrointestinal health

Probiotics

- High yoghurt consumption in Turkish society

	Human nutrition
Goal	Long term effect
Effectiveness	Difficult to assess
Characteristics of Intake	In combination with a small portion of food
Frequency of intake	Once per day or more
Microorganisms	Lactobacillus spp. Bifidobacterium spp. Enterococcus spp.
Natural habitat	Digestive tract, milk product



Probiotics

LACTOBACILLUS SPECIES

L-CASEI

L-RHAMNOSUS

L-ACIDOPHILUS

L-PLANTARUM

L-HELVETICUS

LACTOBACILLUS

Microorganism	Use
Lactobacillus acidophillus	Vaginal infection.
Bifidobacteria	fight against food poisoning bacteria including E.coli. Prevent diarrhoea in children
Lactobacillus GC-	treat antibiotic associated diarrhoea, traveler's diarrhoea and rotavirus infection
Lactobacillus johnsonii	reduce incidence of H. pylori-caused gastritis and may reduce inflammation

Prebiotics

Prebiotics are the substances, which reach to colon in intact form i.e. without getting depleted by the gastric pH and digestive acids.

These prebiotics also selectively promote the growth of colonel probiotic bacteria; hence they act as fertilizers for these bacteria.

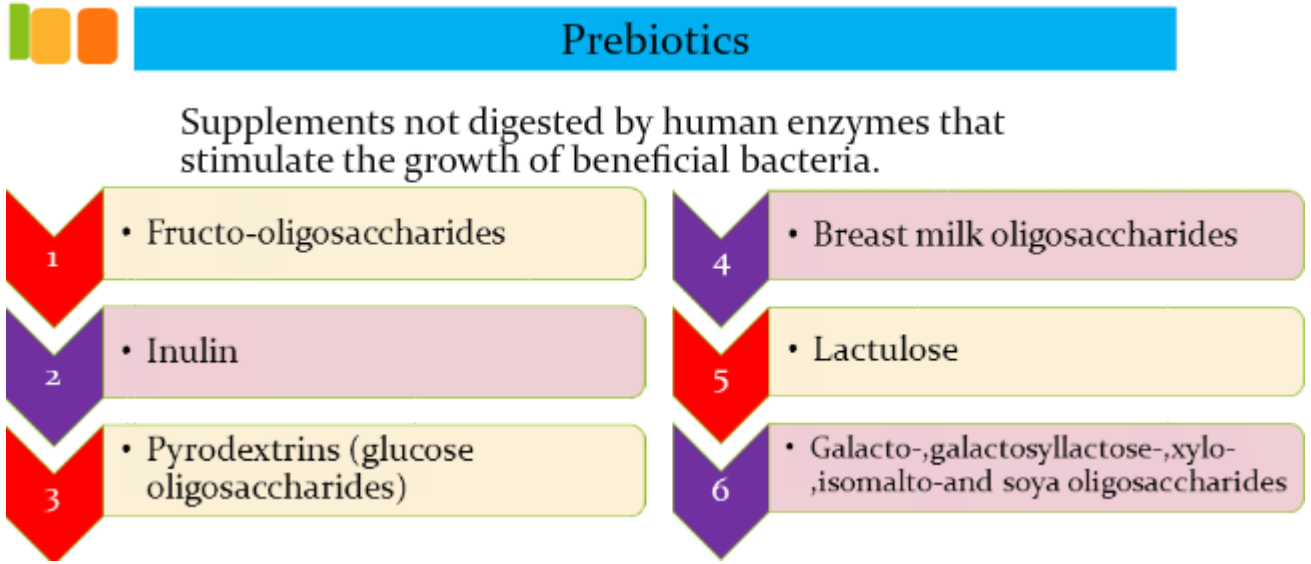
These are collective term for non-digestive but a fermentable dietary carbohydrate that may selectively stimulates growth of certain bacterial groups' resident in the colon, such as *Bifidobacteria, Lactobacilli* considered to be beneficial for the human host.

inulin, which is soluble dietary fibres and resistant to digestive enzyme and thus reaches to large intestine or colon essentially intact, where it is fermented by resistant bacteria, *Lactobacilli.*

- Fructo oligosaccharides
- Inulins
- Lactilol
- Lactulose
- Soybean oligosaccharides
- Lactosucrose
- Isomalto-oligosaccharides
- Gluco-oligosaccharides
- Xylo-oligosaccharides

Prebiotics in functional food

- The largest application for prebiotics in the country is bakery products, including several types of biscuits followed by dairy products, health drinks, nutrition bars, breakfast cereals, flours, jams, and beverages. Prebiotics are also used in dietary supplements (nutritional supplements, specialty nutrients, infant foods) and animal feed probiotics.



Polyunsaturated fatty acids

- Essential fatty acids are needed for normal growth and development but cannot be synthesized by our body
- Omega-3 fatty acids belong to this class.
- Long chain omega-3 fatty acids such as eicosapentaoic acid and docosagexanoic acids are built up in algae and plankton and the fish living on them.
- The natural vegetable oils and marine animal oils containing polyunsaturated fatty acid belong to Linoleic group (omega 6-type and omega 3-fatty acid) help to reduce cholesterol formation/deposition and prevent thromboxane formation.
- EX- safflower oil, corn oil, soybean oil, mustard oil and marine fishes32. Evening primrose oil, flax oil, hemp seed, borage seede33.

Polyphenols / Flavonoids / Anthocyanins

Polyphenols are a class of phytochemicals found in fruits and vegetables.
The most extensively researched polyphenols are flavonoids. Flavonoids constitute a large sub-class of polyphenols with considerable research demonstrating their brain protective and optimizing benefits. Flavonoid-rich foods such as red wine, tea, blueberries and chocolate, are gathering increasing interest and study for their neuroprotective benefits, including neutralizing the effects of neurotoxins on the brain, suppressing inflammation, and boosting memory and cognition.

Fatty Acids

Long chain omega-3 Fatty Acids-DHA/EPA	**Salmon and other fish oils**	**Reduce risk of cardiovascular disease. Improve mental, visual functions**
Conjugated Linoleic Acid (CLA)	**Cheese, meat products**	**Improve body composition. Decrease risk of certain cancers**

Tomatoes and salmon are two types of food that researchers have found to contain benefits beyond basic nutrition — in this case, lycopene and omega-3 fatty acids, respectively.

Safety and Efficacy

Nutraceutical hold great potential as evidence

By products such as benecol , an alternative to margerine that contains plant stanol esters,which have been shown to reduce cholesterol.

They also may hold The potential for harm ,as was the case with ephedrine Widely used botanicals ingredients in wt. loss. The danger is many of these product do not provide Consumer with solid information about their safety and Effectiveness .Hence the policy is required in this matter

Mechanism of action-1

Every nutritional process utilizes a plethora of proteins, such as the digestive enzymes, nutrient transporters, and various enzymes in metabolic pathways.
Proper expression of these proteins underlies the nutrient homeostasis in the cell.
The nutrients themselves can also modulate cell signaling and gene expression. Consequently, studies on the expression of proteins involved in the absorption, distribution, metabolism, and excretion of nutrients, as well as nutrient-mediated expression of genes, form an integral part of the molecular basis of nutrition.

Mechanism of action-2

The ability to study the effects of nutrients on gene expression has been greatly refined and expanded by highthroughput techniques to study global gene expression profiles.
Advances in DNA sequencing technology have also aided in understanding the genetic basis of interindividual differences. Therefore, it is reasonable to hope that such knowledge can be utilized to understand the science of nutritional genomics and the molecular basis of human nutrition as well as individual genetic differences that affect it.

Overview of Nutraceutically relevant transporters

Transporter	*SLC* (gene) family designation	Known substrates	2°Active (Na^+/H^+) or facilitative (F)
SUGAR TRANSPORTERS			
SGLT	*SLC5A*	Glucose, galactose	Na^+
GLUT	*SLC2A*	Glucose, fructose, myo-inositol, glucosamine, dehydroascorbate	F
AA TRANSPORTERS			
AA transporters	*SLC1A, 6A, 7A, 16A, 36A, 38A, 43A*	Amino acids, monocarboxylates (e.g., lactate, pyruvate)	Na^+/H^+/F (depending on the transporter)
PEPTIDE TRANSPORTERS			
PEPT	*SLC15A*	Dipeptides, tripeptides	H^+
FATTY ACID TRANSPORTERS			
MCT	*SLC16A*	Short-chain fatty acids (monocarboxylates; e.g., acetate, lactate, pyruvate, butyrate, propionate, succinate)	H^+
FATP	*SLC27A*	Long-chain fatty acids	
NUCLEOSIDE TRANSPORTERS			
CNT	*SLC28A*	Nucleosides	Na^+
ENT	*SLC29A*	Nucleosides	F
WATER-SOLUBLE VITAMIN TRANSPORTERS			
SVCT	*SLC23A*	Vitamin C (L-ascorbate)	Na^+
SMVT	*SLC5A6*	Biotin, pantothenate, α-lipoate	Na^+
PCFT	*SLC46A1*	Folate, antifolate (e.g., methotrexate)	H^+
RFC1	*SLC19A1*	Folate, antifolate (e.g., methotrexate)	Organic phosphate
THTR	*SLC19A2 and -3*	Thiamine	F
FAT-SOLUBLE VITAMIN TRANSPORTERS			
SR-B1		Vitamin D, vitamin E, lutein, lycopene, cholesterol, cholesteryl esters	
NPC1L1		Vitamin D, vitamin E, cholesterol	

OTHER TRANSPORTERS			
OCTN, CT2	*SLC22A*	L-Carnitine	Na^+/F (depending on the transporter)
TAUT	*SLC6A6*	Taurine	
ZIP	*SLC39*	Metals (e.g., Zn)	
ZnT	*SLC30*	Metals (e.g., Zn)	
Nramp (Nramp1; Nramp2 also known as DCT1/DMT1)	*SLC11A*	Divalent metals and iron	H^+

• Phytochemicals:

1. **Phytochemicals could provide health benefits as:**
2. **Substrate for biochemical reactions**
3. **Cofactors of enzymatic reactions**
4. **Inhibitors of enzymatic reactions**
5. **Absorbents that bind to & eliminate undesirable constituent in the intestine**
6. **Scavengers of reactive or toxic chemicals**

6. **Enhance the absorption and / or stability of essential nutrients**
7. **Selective growth factor for beneficial bacteria**
8. **Fermentation substrate for beneficial bacteria**
9. **Selective inhibitors of deleterious intestinal bacteria**

Hepatic effects of selected nutraceuticals

Compound/ source	Active constituent(s)	Hepatoprotective effects	Hepatotoxic effects	References
Andrographis paniculata	Diterpenes, lactones, flavonoids	↓ lipid peroxidation and hepatocellular damage due to acetaminophen and carbon tetrachloride	–	Akbar (2011)
Areca catechu	Alkaloids, tannins, flavones, triterpenes, sterols, fatty acids	Antioxidant, anti-inflammatory, lipid regulation	–	Peng et al. (2015)
Black cumin (*Nigella sativa*)	Thymoquinone	↑ neoplastic cell apoptosis; antioxidant; protects from cisplatin-induced injury	–	Khan et al. (2011); Al-Malki and Sayed (2014)
Blue green algae (*Spirulina* spp.)	Carotenoids	Antioxidant	Microcystin contamination may result in hepatic injury	Madrigal-Santillan et al. (2014); Jiang et al. (2008)
Capsicum spp.	Capsaicinoids	–	Bioactivation with formation of electrophiles	Reilly and Yost (2006)
Commiphora mukul	Gum guggul	Hypolipidemic, ↓ lipid peroxidation		NTP (2005)
Luteolin	–	↓ expression of lipogenic genes, decreased ethanol-induced steatosis	Bioactivation to reactive metabolites, glutathione depletion	Shi et al. (2015); Liu et al. (2014)
Melatonin	–	↓ lipid peroxidation, ↓ DNA damage, ↓ necrosis, ↓ expression of inducible nitric oxide synthetase	–	Schmidt (2010); Mathes (2010)
Milk Thistle (*Silybum marianum*)	Silibinin (Silybin)	Antioxidant, anti-inflammatory, antifibrotic; ↓ neoplastic cell proliferation, ↑ neoplastic cell apoptosis	Exacerbates tumor promotion effects of ethanol	Loguercio and Festi (2011); Brandon-Warner et al. (2012)
	Silymarin	Antioxidant, anti-inflammatory, ↑ glutathione and superoxide dismutase levels, membrane stabilization, antifibrotic, stimulates hepatocellular regeneration		Bahmani et al. (2015); Madrigal-Santillan et al. (2014)
Neem (*Azadirachta indica*)	Azadirachtin-A	↓ necrosis from carbon tetrachloride; ↓ apoptosis from cisplatin	–	Baligar et al. (2014); Dkhil et al. (2013)
Resveratrol	–	Antioxidant, anti-inflammatory, decreased hepatic triglyceride accumulation	–	Heeboll et al. (2014)

Selected Nutraceuticals that Affect the Cardiac System

Nutraceuticals	Source	Active ingredient	Effect
Cruciferous vegetable	Broccoli, kale	Sulforaphane	Antioxidant
Bulbous plant	Garlic	Allicin	Antihypertensive
Green tea	*Camellia sinensis*	Epigallocatechin gallate	Demethylating agent Antioxidant
CoQ10	Endogenous compound	Ubiquinone, coenzyme	Energy production in cells Vascular function
Turmeric	Ginger family	Curcumin	Anti-inflammatory Reduces oxidized LDL
Grape skin	Red grapes	Resveratol Phytoalexin	Antioxidant Antimolecular sticking
Fish oil	Herring	Omega-3s	Reduces inflammation
Vegetable	Tomato	Lycopene	Antioxidant Endothelial function
Legume	Soy	Phytoestrogen	Reduces LDL Improves vascular function

Nutrients and Nutraceuticals and Their Relevance to Azheimers and Dementia

Nutrient or nutraceutical	Elicited effects
Polyphenols, amyloid-binding polyphenols	Target-specific signaling pathways associated with protein folding and neuroinflammation Inhibit fibril formation or steer oligomer formation
Curcumin, Cur1	Anti-inflammatory and antioxidant effects Activate the heat shock response, reducing oxidative damage Attenuate cognitive impairment and stimulate neuroprotection, inhibit the generation of Aβ by inducing autophagy via downregulation PI3K/Akt and mTOR Protect from exogenous effects of Aβ1–42 via the upregulation of hTERT expression
Isoflavones (e.g., genistein, GS-14, 25d)	Elicit neuroprotection from Aβ protein exposure, inhibits AChE, modulates estrogenic activity Antioxidative activity, inhibit Aβ aggregation and exhibit metal chelating properties; reverse scopolamine-induced memory deficit Attenuate cytotoxicity and inflammatory damage induced upon Aβ25–35 exposure by inhibiting TLR4 and NF-κB upregulation
Isothiocyanates (e.g., sulforaphane)	Activate Nrf2/ARE pathway, promoting the upregulation of GSH Antioxidant potential upon exposure to Aβ25–35, upregulate antioxidant enzymes via activation of Nrf2, prevent Aβ-mediated apoptosis
Folate, vitamin B12, vitamin B6	Prevent tau hyperphosphorylation and memory deficits induced by acute administration of homocysteine Inhibit tau hyper-phosphorylation and accumulation in hippocampus and cortex; downregulate GSK-3β, CDK5, JNK, ERK, and p38MAPK, attenuate memory deficits No improvements of primary and secondary cognitive measurements, depression as adverse effect Ineffective for AD or dementia
Fortasyn Connect™ (cocktail of docosahexaenoic acid, eicosapentaenoic acid, uridine-5'-monophosphate, choline, phospholipids, antioxidants, and B vitamins)	Designed to enhance synapse formation and functionality Improve memory performance, positively affect brain functional connectivity
Shilajit, fulvic acid, with/without B vitamins	Contribute to AD prevention
Vitamin E, vitamin C, α-lipoic acid (E/C/ALA)	Lower CSF F2-isoprostane levels, indicative of oxidative stress reduction in the brain but associated with faster cognitive decline
γ- and α-Tocopherols	High α-tocopherol seems to be associated with higher amyloid load when γ-tocopherol levels were low Conversely, high α-tocopherol seems to be associated with lower amyloid levels when γ-tocopherol levels were high
SAM, PUFAs	Neuroprotective (particularly SAM) under conditions of reduced GST activity, diminished SAM, increased accumulation of SAH, and deprived folate

Nutraceuticals with Antiatherosclerotic and Antiatherogenic Activity

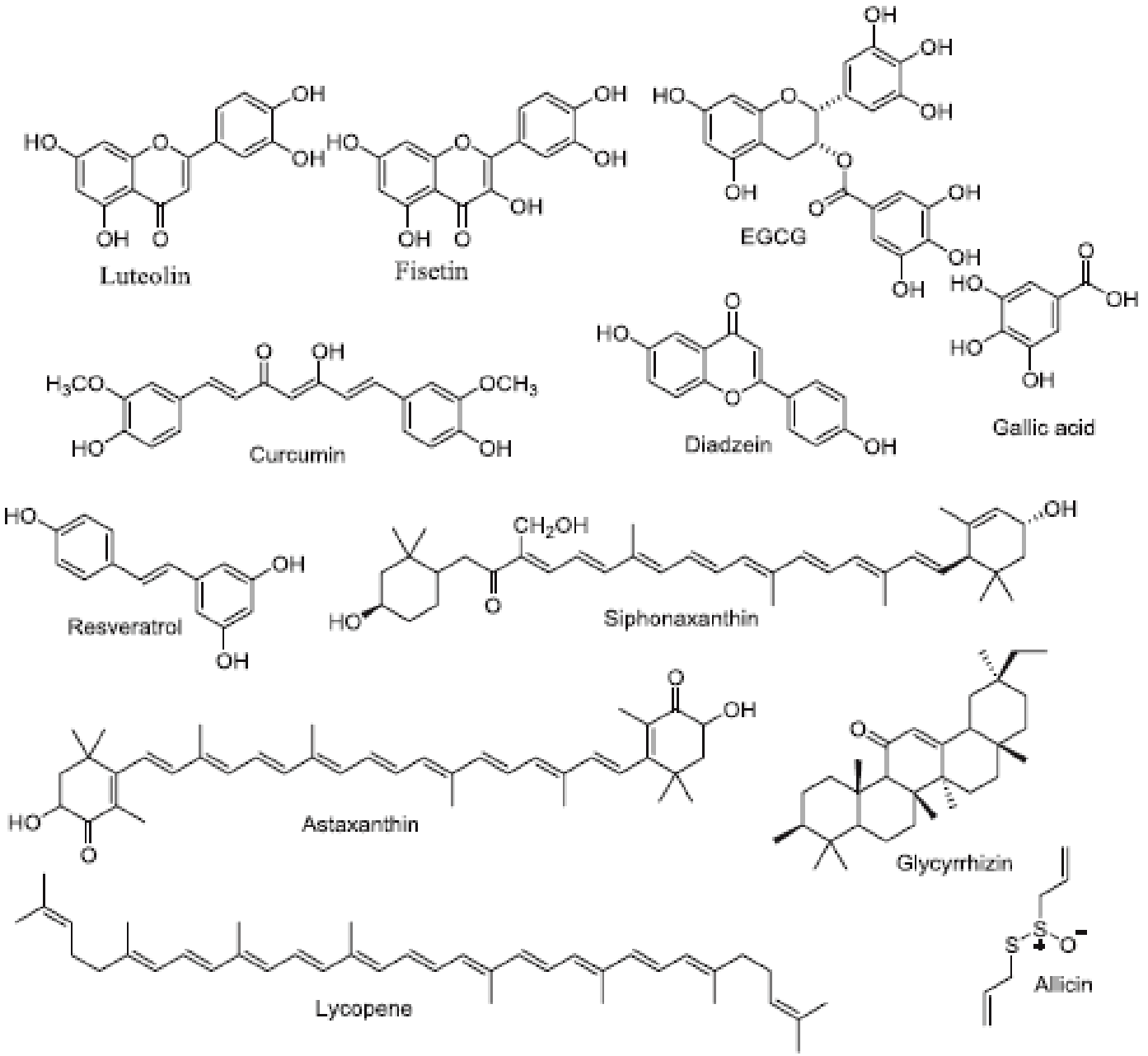
Nutraceutical	Source(s)	Antiatherosclerotic activity
ANTIATHEROGENIC (PREVENTIVE)		
Monounsaturated fatty acids (omega-9)	Olive oil	Improve plasma lipid profile, ↑HDL, ↓cholesterol, improve endothelial function, inflammation, ↓blood sugar, ↓body weight
Polyunsaturated fatty acids (omega-3, omega-6)	Fish, sea products, walnuts, cereals, vegetable oil	↓Plasma triglycerides, ↓platelet aggregation, ↑endothelial NO production, ↓blood pressure, prevent arrhythmias, (efficacy questioned)
Polyphenols	Olive oil, wine, tea, vegetables, fruits	↑HDL, ↓LDL, ↓cholesterol trapping, ↓LDL oxidation, ↓plaque formation, improve endothelial function, ↑NO production, modulate inflammation, ↓platelet aggregation
Phytosterols and phytostanols	Vegetable oils, nuts, fruits, vegetables	↓Cholesterol, additive effects with statin therapy, supplementation of various foods
Anti-inflammatory agents	Medicinal herbs	↓Inflammation, modulate the cellular activation processes leading to the atherosclerotic plaque formation
Dietary fiber	Grain, cereals	↑HDL, ↓body weight, ↓blood pressure in high-risk patients
Antioxidants/vitamins	Fruits, vegetables, herbs	General effect in the prevention of atherosclerosis development, anti-inflammatory effects
ANTIATHEROSCLEROTIC (THERAPEUTIC)		
Active components of garlic	Garlic (raw, powder, aged extract)	↓Cholesterol retention, improve lipid metabolism, ↓formation and ↑degradation of cholesterol esters, antioxidant properties
Phytoestrogens	Medicinal herbs, vegetables, red wine, tea, soybean	Improve vascular function, ↓plaque formation, ↓LDL, modulate inflammation, ↓platelet aggregation

Note: LDL, low-density lipoprotein; HDL, high-density lipoprotein; NO, nitric oxide.

Renal Effects of Nutraceuticals

Compound/source	Active constituent(s)	Renal effects
Astragalus membranaceus, Astragalus mongholicus	Astragalosides	Diuretic; antioxidant; anti-inflammatory; attenuates complement-mediated podocyte injury; reduced proteinuria in patients with diabetic nephropathy; improved GFR
Blue green algae (*Spirulina* spp.)	Carotenoids	Antioxidant; ↓ injury due to cisplatin and gentamicin
Conjugated linoleic acid	–	Worsened renal hypertrophy, glomerular and interstitial fibrosis, and inflammation in obesity-associated nephropathy
Cordyceps sinensis	H1-A	Antioxidant
Licorice (*Glycyrrhiza glabra*)	Glycyrrhizin	Reduced proteinuria; immunomodulation; inhibition of mesangial sclerosis and inflammation; promotes lowered potassium
Milk thistle (*Silybum marianum*)	Silymarin, silicristin	Antioxidant; mitigates ischemia-perfusion injury; reduced damage due to diabetic nephropathy; enhances glutathione system function; stimulates renal epithelial regeneration *in vitro*
Neem (*Azadirachta indica*)	Aqueous extract	Modulation of nitric oxide (NO); antioxidant; reduces apoptosis of renal cells
Rhubarb (*Rheum* spp.)	Emodin, rhein	Decreased BUN, creatinine; reduced degenerative changes in glomeruli and tubules

Clinically important nutraceuticals for treating GI disorders



Nutraceuticals in Male Fertility

Nutraceuticals	Dietary sources	Clinical benefit
Arginine	Food grains, coconut, dairy, nuts, seeds, meats	Protective effects against oxidative damage, improve sperm quality and production
Astaxanthin	Salmon/fish/yeast	Improve sperm parameters and fertility
Carnitine	Fish, poultry, red meat, dairy products	Improve serum functional quality
Coenzyme Q10	Whole grains, nuts, onions, rice bran, potatoes, soybeans, spinach, oily fish, cabbage, carrots,	Improve serum quality
Folic acid	Avocado, beans, brewer's yeast, cereals, citrus, eggs, dark green leafy vegetables, meats	Improve serum quantity characteristics, quality, and function
Glutathione	Fruits, vegetables, meats	Protective effects against oxidative damage/ROS
Lycopene	Tomato	Protective effects against oxidative damage, improve serum quality
Omega fatty acids	Fish, nuts, oils	Induced sperm count, motility, and morphology
Selenium	Cereal, eggs, nuts, meat, seafood	Improve semen parameters and fertility
Vitamin A	Carrots, cruciferous vegetables, pumpkin, sweet potatoes, dairy, eggs, oily saltwater fish, meat	Spermatogenesis
Vitamin C	Fruits (citrus, kiwi, papaya, strawberry, and others) and vegetables (bell pepper, broccoli, cauliflower, kale, and others)	Improve semen quality
Vitamin E	Fruits, vegetables, cereals, grains, vegetable oils, wheat germ, eggs, dairy	Improve semen quality
Zinc/magnesium/ calcium	Pumpkin seeds, sesame seeds, sunflower seeds, wheat	Serum quality

Bioactive compound foods grown in Turkey that are used for their various potential benefits are

- Amaranthus (*Amaranthus* spp.), caper (*Capparis spinosa*), chicory (*Cichorium intybus* L.), coriander (*Coriandrum sativum* L.), cumin (*Carum carvi* L.), dandelion (*Taraxacum officinale* L.), fennel (*Foenicilum culgare* L.), flaz (*Linum mucronatum*), mallow (*Malva sylvestris* L.), marjoram (*Origanum onites* L.), milk thistle (*Silybum marianum* L.), nettle (*Urtica urens/diotica* L.), purslane (*Portulaca oleracea*), rocket (*Eruca sativa*), rosemary (*Rosmarinus officinalis* L.), sage (*Salvia officinalis* L.), savory (*Satureja hortensis*), Spanish lavender (*Lavandula oechas* L.), Spanish salsify (*Scolymus hispanicus*), sweet basil (*Ocimum basilicum* L.), thyme (*Origanum vulgare* L.), wild mustard (*Sinapis arvensis* L.), and wild radish (*Raphanus raphanistrum*)

Marine Nutraceuticals

- Marine-derived nutraceuticals are alternative sources for synthetic ingredients that can contribute to consumers' well-being and play a vital role in human health and nutrition

Marine Nutraceuticals-2

- As one of the most important sources of nonanimal sulfated polysaccharides, marine algae have been used for various ailments. There are studies concerning the antimicrobial and antifungal activities of marine algae collected from Turkey, such as Phaeophyceae (*Dictyopteris membranaceae*, *Cystoseira barbata*, *Cystoseira compressa*, *Cystoseira mediterranea*, *Halopteris scoparia*, *Dictyota dichotoma*, *Colpomenia sinuosa*, *Ectocarpus siliculosus*, *Padina pavonica*, *Dictyota linearis*), Rhodophyceae (*Jania rubens*, *Acanthophora najadiformis*, *Laurencia papillosa*, *Hypnea musciformis*, *Gracilaria gracilis*, *Ceramium rubrum*), and Chlorophyceae (*Enteromorpha linza*, *Ulva rigida*)

Marine Nutraceuticals-3

- Even though no suppliers for marine algae are present, white fish oil, cod oil, and omega-3 fish oil are currently being marketed in Turkey.
- Eicosapentaenoic acid and docosahexaenoic acid are the two most beneficial omega-3 fatty acids found in oily fish and fish oil supplements. These are essential to maintain the balanced production of hormone-like substances that help regulate many important physiological functions, including blood pressure, blood clotting, nerve transmission, inflammatory and allergic responses, functions of the kidneys and gastrointestinal tract (GIT), and the production of other hormones

Fermented Products as Nutraceuticals

- Ayran *Streptococcus thermophilus* and *Lactobacillus delbrueckii* subsp. *Bulgaricus*

- Kefir, ethnologically derived from two Turkish words “köpür,” meaning “foamy,” and “keyif,” meaning “good feeling”, is beneficial to the immune system, gastrointestinal system, and cholesterol metabolism, and has antitumoral, antibacterial, and antifungal properties.
- Recently, antihyperlipidemic and antihyperglycemic effects as well as improved efficacy and tolerability of triple therapy in eradicating *Helicobacter pylori* were shown

- “Shalgam (salgam)” is the traditional beverage produced from the lactic acid fermentation of black carrot, aromatic turnip (celem), rock salt, sourdough, bulgur flour, and drinkable water served cold in large glasses.
- Shalgam juice fermentation is mainly performed by lactic acid bacteria (LAB). The main species isolated in the fermentations of shalgam are *Lactobacillus plantarum* and *Lactobacillus paracasei* subsp. *paracasei*. Significant growth of *Lactobacillus brevis* and *Lactobacillus fermentum* was also observed during the fermentations depending on the production plant, and *Leuconostoc mesenteroides* subsp. *mesenteroides*, *Pediococcus pentosaceus*, and *L. delbrueckii* subsp. *delbrueckii* were isolated at the beginning of fermentation, which did not grow and died

- “Boza” is defined by the Turkish Standards Institution (TSE) (TS 9778) as “A product which is made by addition of water to cereals such as millet, maize, wheat, and rice.” This yeast and lactic acid fermentation creates a highly viscous and low-alcoholic liquid with a pale yellow color and sweet/ sour taste (*Lactobacillus acidophilus* LA-5 and *Bifidobacterium bifidum*
- BB-12 and *Saccharomyces boulardii*)
- This culturally popular drink has beneficial effects because bozarelated LAB, bacteriocins, or bacteriocin-like peptides were found to possess antifungal and antibacterial activitie.
- Protein hydrolysate, fractionated hydrolysates, and dialysates obtained following *in vitro* digestion of boza were found to contain bioactive compounds vented as a good source of angiotensinconverting enzyme inhibitory peptidess

Digestive enzymes

- As we ages, stomach cell responsible for acid production slow down, this in turns slow the transit time of food in the stomach causing reflux of food from the esophagus.
- Pepsin protein
- Amylase carbohydrate & sugar
- Betaine HCl phase I digestive aid
- Pancreatin, an enzyme from pancreas is often found in enzymatic formulation.
- Papain plant proteolytic enzyme obtained from carica papaya fruits
- Bromelain from stem & fruit of pineapple.

Sports Nutritionals

- Sports nutritionals, including sports drinks and nutritional bars, and other products such as protein and weight gain powders, supplements for before and after workouts, and energy gels are an increasing trend driven by the consumer demand for healthier, more dynamic sports beverages.
- To help athletes replace water and electrolytes, energy isotonic, hypotonic, and hypertonic beverages are currently marketed.
- These products and other supplements, such as protein (PRO), amino acid (AA), or carbohydrate (CHO) supplements, are defined by the Turkish Food Codex-Sports Food Regulation (2003/42).

Energy drinks

- As per the Turkish Food Codex Energy Drinks Communiqué no. 26309 (number 2006/47), in Turkey, energy drinks are defined as “Energy-providing drinks including functional substances, vitamins, and minerals which are defined in product properties for human consumption due to usable carbohydrates in its content.”
- Energy drinks provide mental and physical stimulation through their stimulant ingredients, which mainly include caffeine; however, other herbal stimulants (e.g., guarana, yerba mate), simple sugars (e.g., glucose, fructose), naturally formed glucose metabolite (glucuronolactine), amino acids (e.g., taurine, carnitine, creatine), herbs (e.g., *Ginkgo biloba*, ginseng), and vitamins may be included.

Regulation of nutraceuticals

- Regarding EU harmonization, the Turkish Government issued a new law, no. 5996, on “Veterinary Services, Phytosanitary, Food, and Feed” on June 13, 2010 (Turkish Official Gazette. No. 27610), with the objective of protecting and ensuring public health, food and feed safety, animal health and welfare, plant health, and consumer interest by taking into consideration environmental protection.
- In the past, veterinary services, phytosanitary, and food and feed policies were covered by separate laws and regulations. Unlike the old bills, law 5996 is related to veterinary services, plant wealth, food and bait requirements, conditions for food safety, food codex, food hygiene, risk analysis, and traceability as concepts that have to be applied in the food industry.

- There are five public institutions and one semi-public institution with relevance to food quality and safety in Turkey
- The Ministry of Food, Agriculture, and Livestock,
- the TSE,
- Turkish Patent Institute,
- Under-Secretary for Foreign Trade
- Turkish Accreditation Agency

- The law has authority over the principles and procedures relating to the production, packaging, sale, import, and export of spring water, drinking water, natural mineral water, and water for medical purposes and the principles and procedures relating to compliance with technical and hygienic rules, ensuring fulfillment of quality standards and monitoring and control of quality standards of potable and utility water to the Ministry of Health.
- The Ministry of Health is also responsible for the principles and procedures relating to the production, import, export, and control of dietary foods for specific medical purposes

- For the implementation of law 5996, the Ministry of Agriculture and Rural Affairs was extensively reorganized by decree law no. 639 on June 8, 2011 (Turkish Official Gazette No. 27958).
- Currently, the Ministry of Food, Agriculture, and Livestock is the competent authority with regard to food and feed safety, veterinary, and phytosanitary issues in Turkey

- In Turkey, nutraceuticals are listed as “food supplements” in Food Law 5996. This covers vitamins, minerals, other substances such as amino acids, essential fatty acids, various plants, and herbal extracts, whether single or in mixtures.

- In addition to this, “Regulation on the import, export, production, processing of food supplements, and their placing on the market” was published in the Turkish Official Gazette (No. 28635) on May 2, 2013, by the Ministry.

TABLE 69.1 List of Food Supplements Licensed by the Ministry of Food, Agriculture, and Livestock after January 13, 2014, to May 4, 2015

	Licensed product number	Product name	Main content	Main nutraceutical benefit
1	2	Shavergrass powder	*Equisetum arvense*	Silisium supplement for antiaging, antihypertensive, antiulcerative
2	2	Vitamin C	Vitamin C	Antioxidant, general health supplement
3	4	Coriander oil	*C. sativum*	Antiaging, anti-inflammatory, antimicrobial, diabetes, sexual enhancement
4	3	Selenium	Selenium	Antioxidant, general health supplement, cancer prevention
5	2	Pomegranate fruit oil	*Punica granatum*	Antioxidant, anticholesterol
6	2	Black cumin oil	*Nigella sativa*	Antiaging, anticancer, gastrointestinal health, antimigraine, antidiabetic
7	2	Wheat germ oil	*Triticum vulgare*	Antioxidant
8	4	Ginger extract	*Z. officinale*	Antiemetic, cancer prevention, antidiabetic
9	7	Curcumin (Turmeric) extract	*Curcuma longa*	Musculoskeletal disease prevention, anti-inflammatory
10	3	Saw palmetto berry extract	*Serenoa repens*	Gastrointestinal health, against chronic cough, cancer prevention
11	1	TA 65®	Cycloastragenol	Antiaging
12	3	Folic acid	Folic acid	Pregnancy, nervous system
13	2	Woundwort extract	*Lavandula stoechas*	Gastrointestinal health, antinociceptive, expectorant
14	4	St. John's wort	*Hypericum perforatum*	Mental health (antidepression)
15	3	Ginseng extract	*Panax ginseng*	Mental health, cardiovascular system
16	2	Fenugreek seed extract	*Trigonell foenum- graecum*	Menopause symptomatic treatment
17	2	Broccoli extract	*Brassica oleracea var. italica*	Anticancer, treatment of autism
18	3	Garlic extract	*Allium sativum*	Anti-inflammatory, cardiovascular system, cancer prevention
19	4	Reishi mushroom extract	*Ganoderma lucidum*	Immune system enhancing, cancer prevention, antidiabetic
20	2	Spirulina extract	*Arthrospira platensis*	Weight control, antioxidant
21	3	Olive leaf extract	*Olea europaea*	Antioxidant, antidiabetic, immune system enhancing
22	1	Vitex fruit extract	*Vitex agnus-castu*	Menopause symptomatic treatment, menstrual cycle

23	2		Devil's weed extract	*Tribulus terrestris*	Male virility and general vitality
24	1		Brown sea weed	*Ascophyllum Nodosum*	Antiaging, gastrointestinal health, general vitality
25	1		Large cranberry extract	*Vaccinium macrocarpon*	Urinary tract infections
26	9		Probiotic	Several probiotic microorganisms in different combination/concentration	Gastrointestinal health, general vitality
27	1		Chlorella algae extract	*Chlorella pyrenoidosa*	Cancer prevention, stimulate immune system
28	2		Flax seed oil	*Linum usitatissimum*	Omega-3 source, gastrointestinal support, cardiovascular disease prevention, blood sugar control
29	1		Chitosan capsule	Chitosan	Weight control
30		2	Magnesium	Magnesium	Bone–muscle health, gastrointestinal health, cardiovascular health
31		7	Fish oil	Omega-3	Cardiovascular health, nervous system health, antioxidant
58		2	Carob tree syrup	*Ceratonia siliqua*	Gastrointestinal health, weight management

32	1	Fish oil and krill oil mix	Omega-3	Cardiovascular health, nervous system health, antioxidant
33	1	Red krill oil *(Euphausia superba)*	Omega-3	Cardiovascular health, nervous system health, antioxidant
34	8	Vitamin and mineral	Vitamin-mineral complex	Support immune system
35	2	Fig extract	*Ficus carica*	Gastrointestinal health (pediatric)
36	2	Choline stabilizing ortosilisic acid	Ortosilisic acid	Atherosclerosis, Alzheimer, immune system enhancement, collagen synthesis
37	3	Milk thistle extract	*S. marianum*	Hepatoprotective
38	4	Propolis support	Bee resin	Antioxidant
39	4	Artichoke leaf extract	*Cynara scolymus*	Reduction of cholesterol levels, gastrointestinal health
40	1	Salai extract	*Boswellia serrata*	Anti-inflammatory
41	4	Nettle extract	*Urtica dioica*	Urinary health, arthritis
42	2	Vegetable oil support	Mixture of several natural vegetable oils	Gastrointestinal health
43	2	Devil's claw extract	*Harpagophytum procumbens*	Cardiovascular health
44	1	Prebiotic fiber	Polydextrose	Gastrointestinal health
45	1	Narrowleaf plantain liquid extract	*Plantago lanceolata*	Wound healing
46	1	Licorice root liquid extract	*Glycyrrhiza glabra*	Gastrointestinal health, antipyretic, antitussive, mucolytic
47	1	Rosemary liquid extract	*R. officinalis*	Analgesic, diuretic, strengthening
48	2	Ginkgo liquid Extract	*Ginkgo biloba*	Antioxidant
49	1	Black grape seed liquid extract	*Vitis vinifera*	Antioxidant
50	1	White peony extract	*Paeonia officinalis*	Antihemorrhoidal and treatment of anal fissure
51	1	NemolixC3	Eggshell membrane, Sunflower seed oil, bovine gelatin, frankincense, turmeric	Antiaging, antioxidant
52	1	Bee pollen	Bee pollen	Antioxidant
53	1	Pycnogenol (pine bark extract)	Pycnogenol	Antioxidant
54	1	Glucosamine sulfate	Glucosamine sulfate	Antirheumatic
55	1	Thyme extract	*Thymus vulgaris*	Respiratory health, anti-inflammatory
56	1	Coenzyme Q-10	Coenzyme Q-10	Cardiovascular health, cancer treatment, antioxidant
57	2	Pumpkin seed oil	*Cucurbita pepo*	Anti-inflammatory, urinary health, gastrointestinal system

- Turkey has wide endemic flora, compromising many genetic resources that are potential sources of nutraceuticals and hytopharmaceuticals. In the near future, not only a growing interest in phytomedicine on multidisciplinary scientific fields, but also the potential interest of consumers, would lead governmental authorities to expand research areas and adjust regulations, which would also add standardization and quality to plant and other animal source materials

- Due to its geographical position and cultural heritage, Turkish cuisine has been influenced by Europe, Asia, the Middle East, and Africa, where fermented foods and probiotics (such as yogurt) have always been a part of daily life
- Regulations regarding the quality and safety of nutraceuticals and functional foods are expected to be formed in accordance with the local needs

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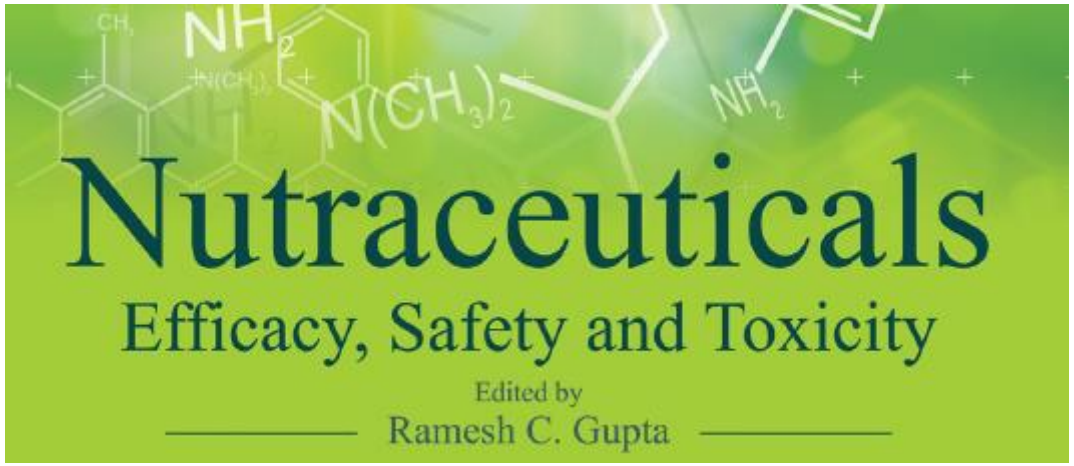

CHAPTER

69

Nutraceuticals: Turkish Perspective

Begum Yurdakok Dikmen and Ayhan Filazi

CONCLUSION

- Nutraceuticals are present in most of the food ingredients with varying concentration
- Concentration, time and duration of supply of nutraceuticals influence human health

- Manipulating the foods, the concentration of active ingredients can be increased
- Diet rich in nutraceuticals along with regular exercise, stress reduction and maintenance of healthy body weight will maximise health and reduce disease risk

- Due to its geographical position and cultural heritage,
- Turkish cuisine has been influenced by Europe, Asia, the
- Middle East, and Africa, where fermented foods and
- probiotics (such as yogurt) have always been a part of
- daily life.
- There is great trend for nutraceuticals and
- functional foods because of consumers interested in
- healthier food, and there are many products with several
- acclaimed health benefits (energy balance, cancer

- Regulations regarding the quality and safety of nutraceuticals
- and functional foods are expected to be formed
- in accordance with the local needs, and not just as a reflection
- of EU commodities. For this purpose, the Ministry
- of Health and the Ministry of Food, Agriculture, and
- Livestock should work together to create an updated
- list of nutraceuticals and food supplements and publish
- this for public commodities. Distribution and marketing
- strategies should be clarified and the public should be
- enlightened about the benefits.